The American Journal of Surgery

EDITED BY THURSTON SCOTT WELTON, M.D.

August 1942

Genitourinary Surgery . Anesthesia

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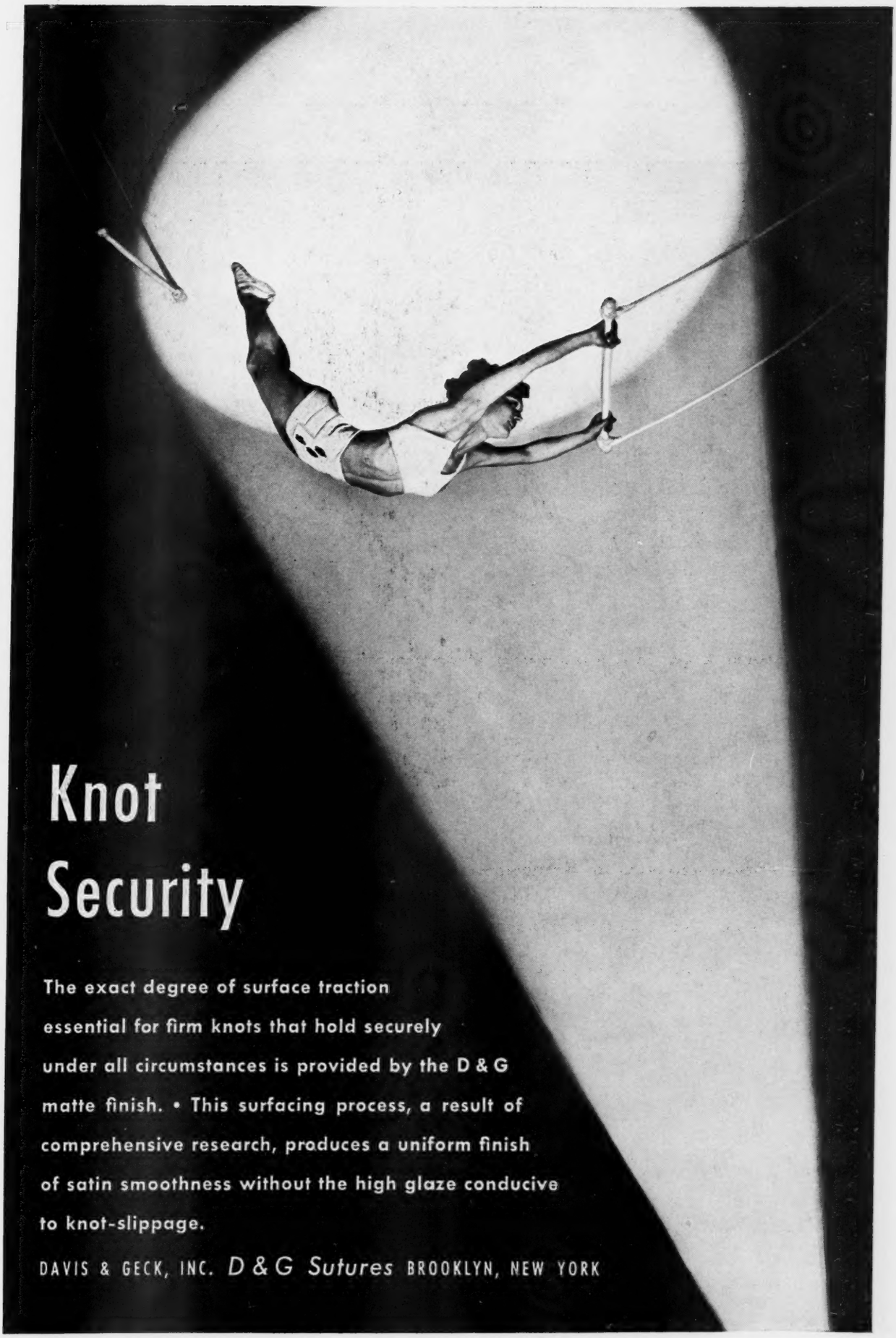

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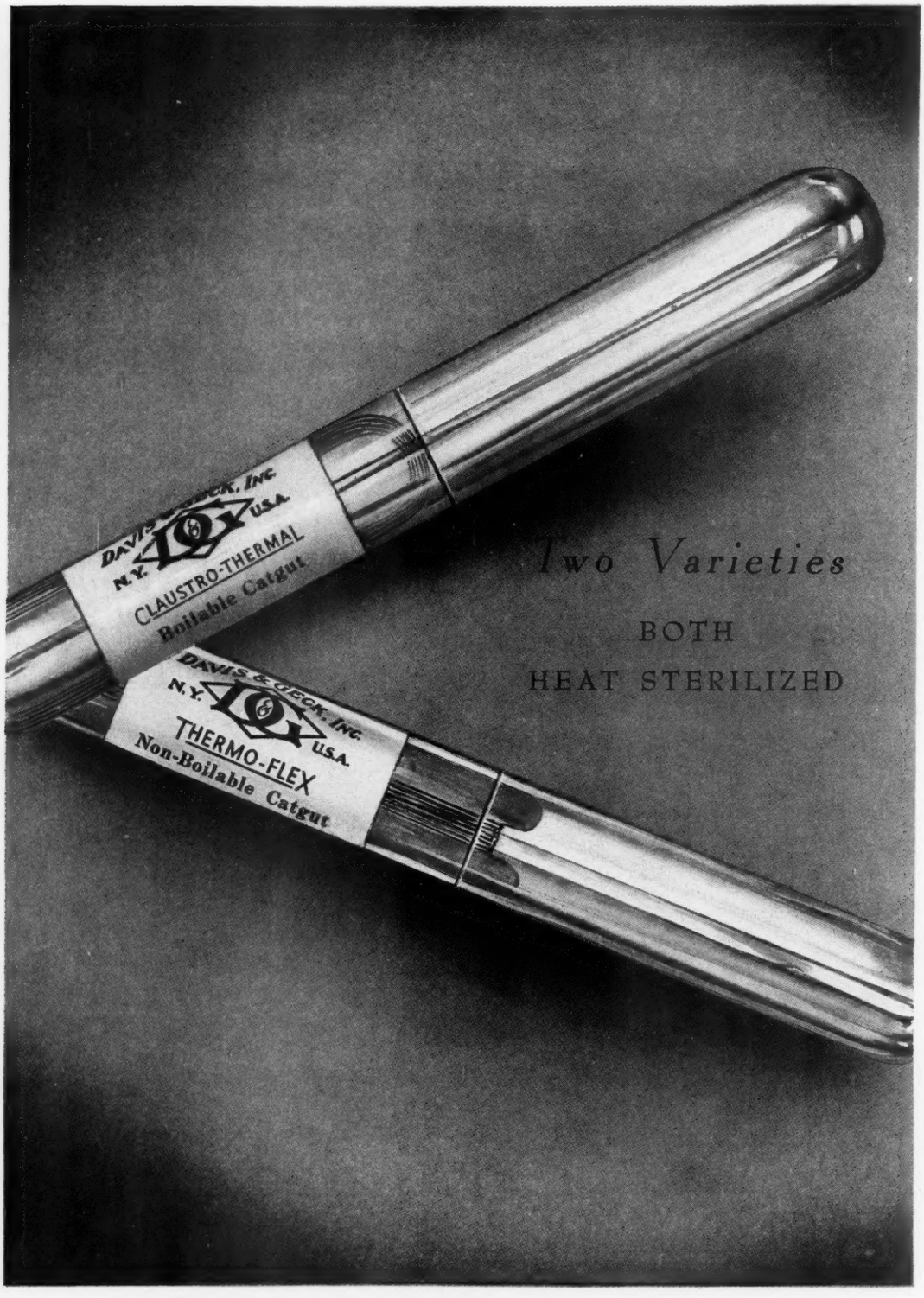

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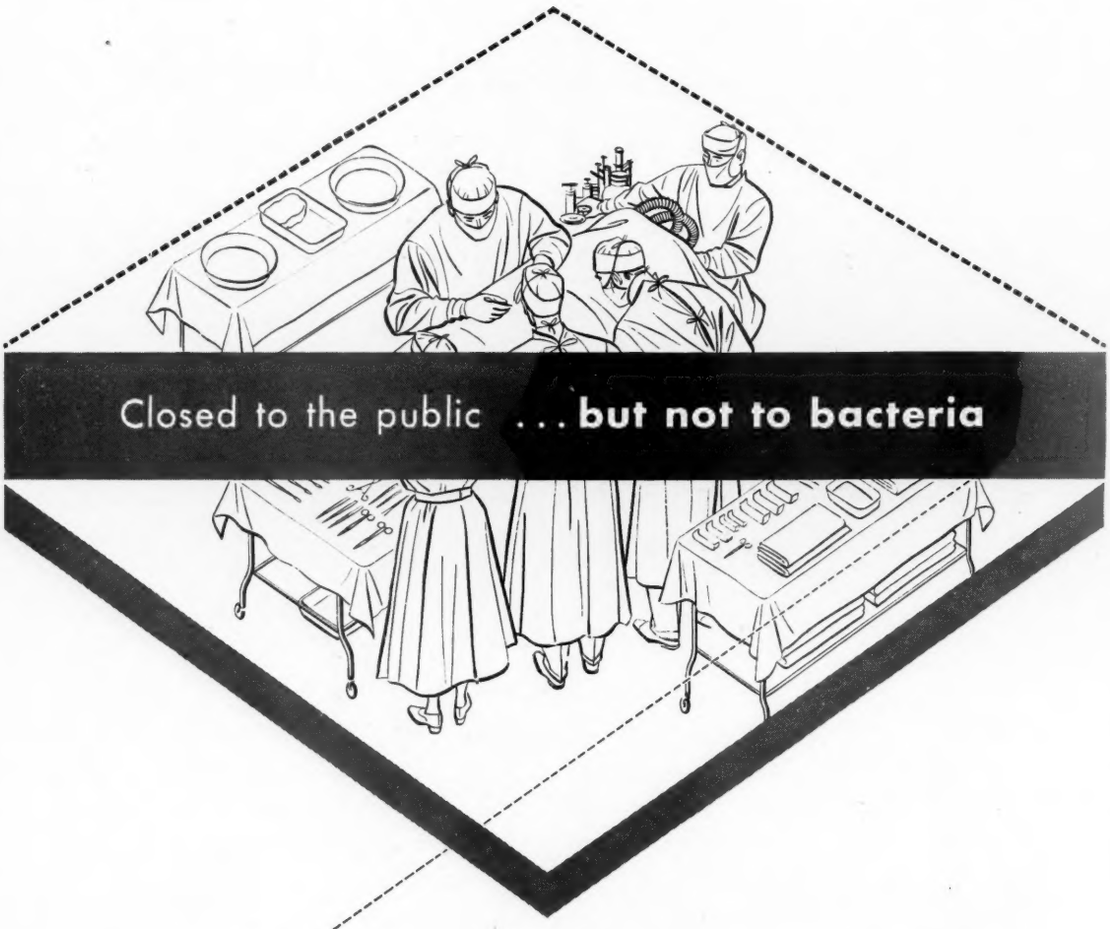

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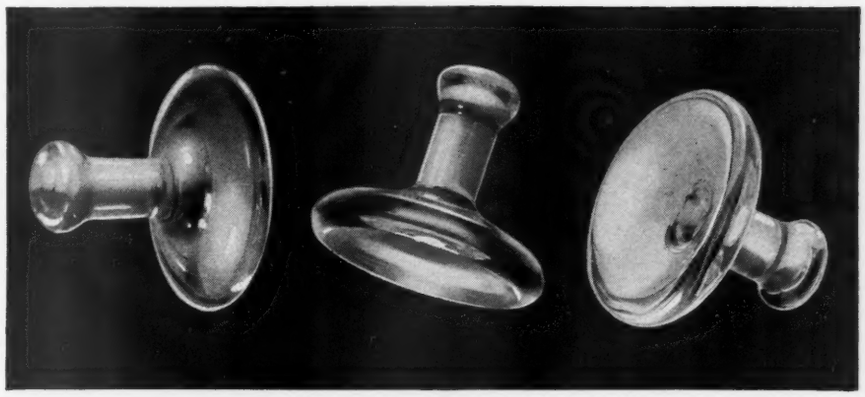

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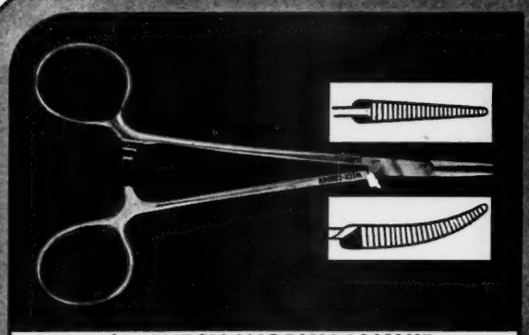

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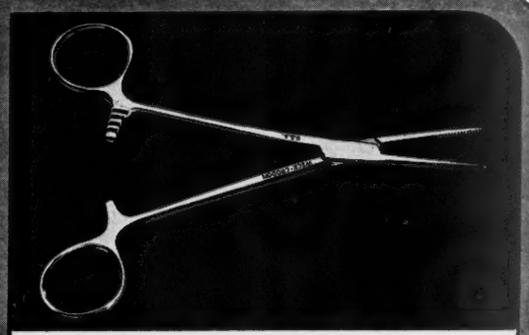

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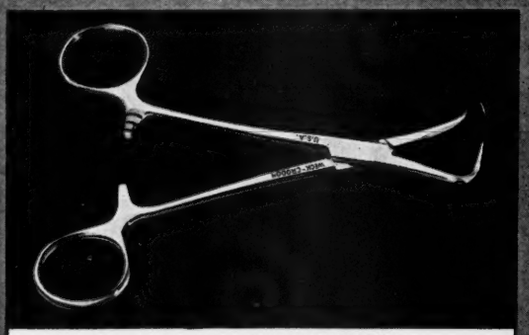

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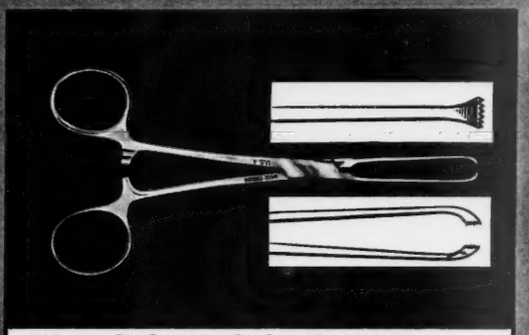

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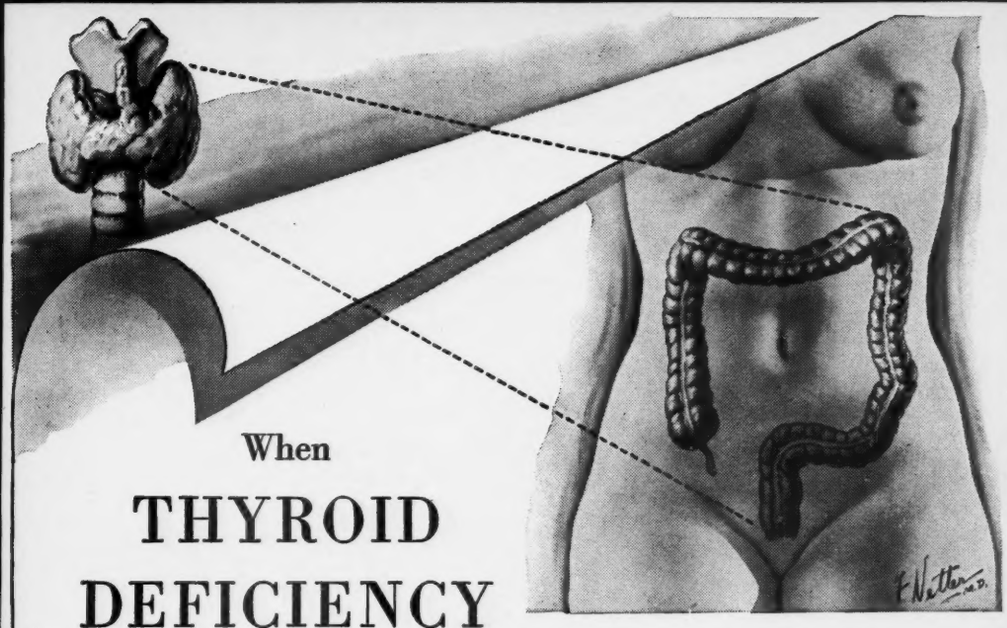

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(1) *Means, J. H.: The Thyroid and Its Diseases; Lippincott; 1937—p. 535.*

(2) *Morest, F. S.: Mississippi Valley Med. J.: Vol. 63. No. 1 (Jan., 1941).*

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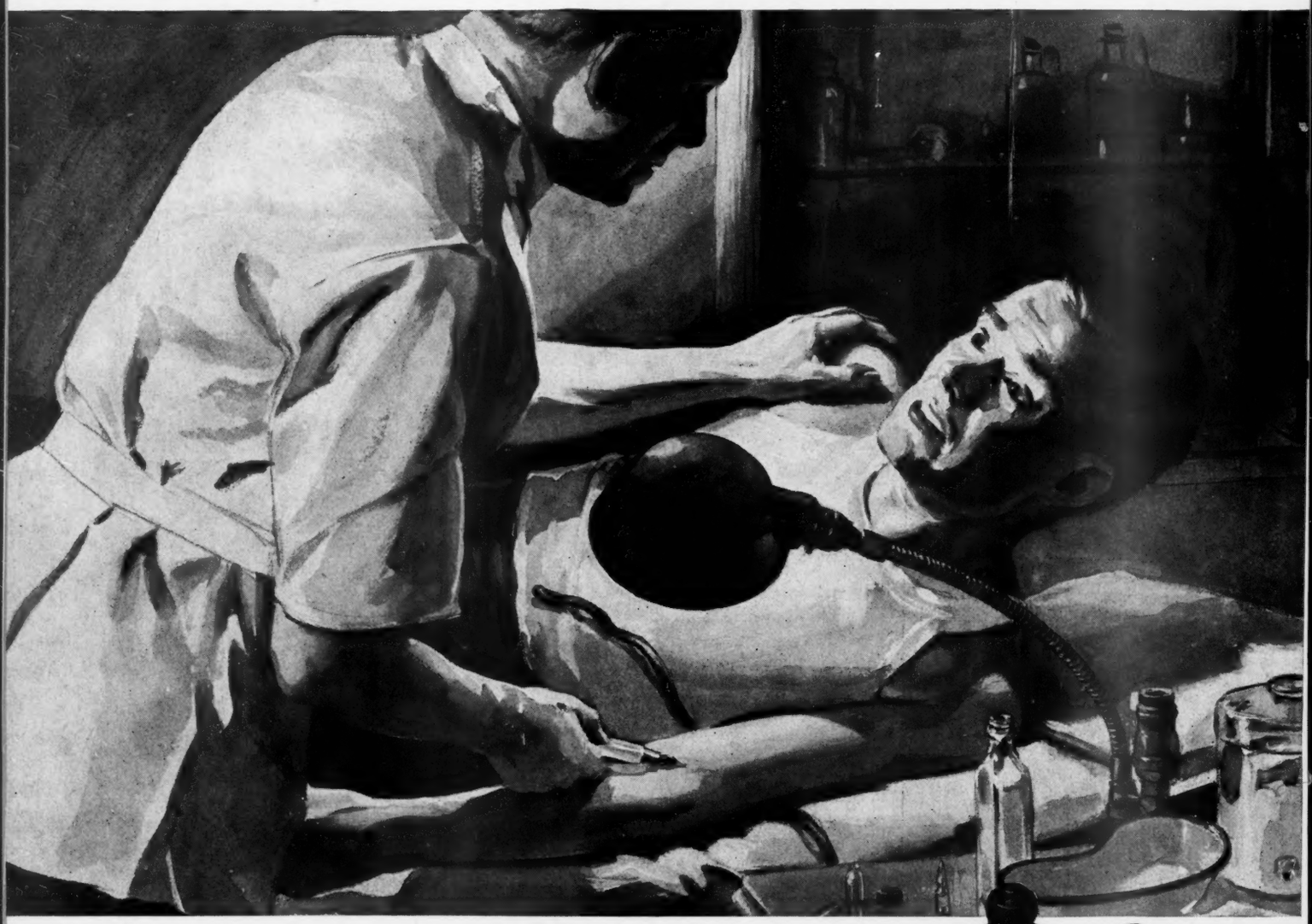

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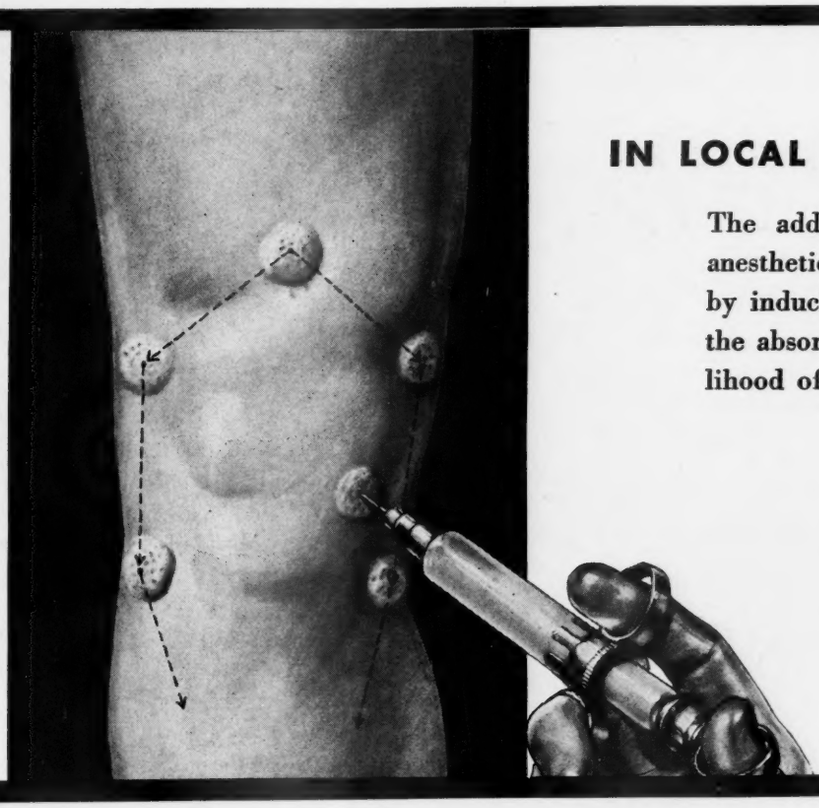

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*Goldzieher, M. A.—"Practical Endocrinology", New York, Appleton-Century, 2nd edition, 1937, page 68.

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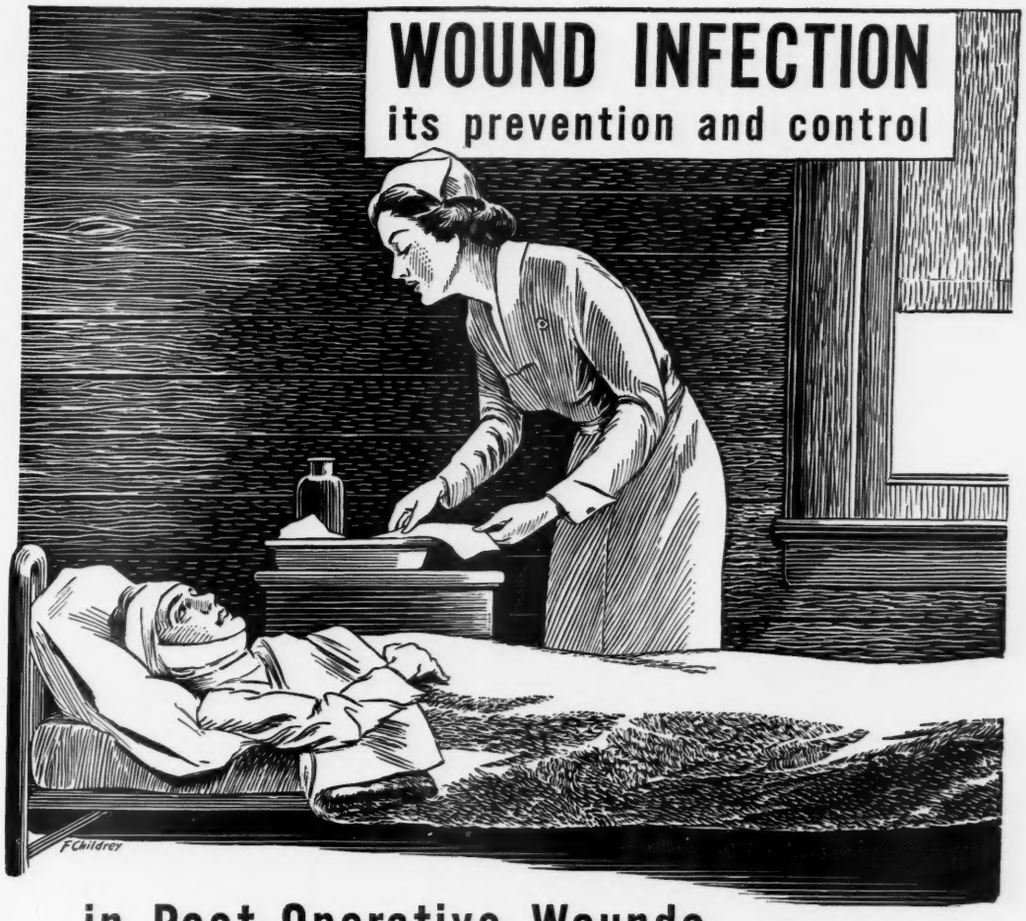

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REFERENCES: Proc. Soc. Exper. Biol. and Med. 48:129, Oct., 1941
Arch. Surg. 44:187, Feb., 1942
Arch. Surg. 44:208, Feb., 1942
Ann. Surg. 115:829, May, 1942
J. A. M. A. 119:615, June 20, 1942

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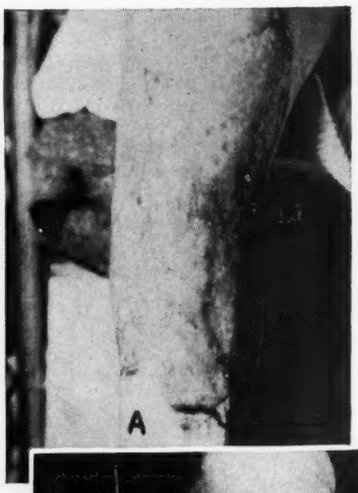

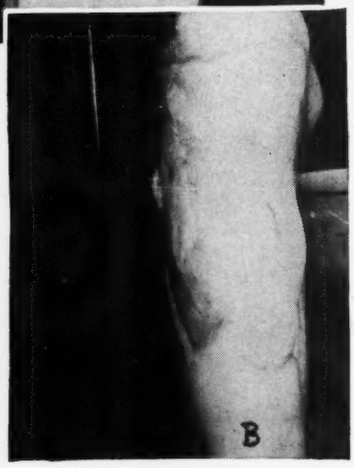

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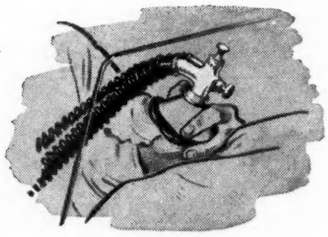

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A PRACTICAL JOURNAL BUILT ON MERIT

NEW SERIES VOL. LVII AUGUST, 1942 NUMBER TWO

Editorial

ACUTE CONDITION OF THE GALLBLADDER

An acute condition of the gallbladder may consist of a spasm of the wall, it may be a pericholecystitis or it may be the sequel of this disorder. If the organ is surrounded by adhesions of the omentum, possibly of available neighboring intestines, there may be necrosis of the wall with leakage and the formation of a neighboring abscess, or the gallbladder may be gangrenous with death of the entire organ.

The diagnosis of an acute condition of the gallbladder obviously is a very difficult problem. The spasm of the gallbladder is a very unpleasant experience as any patient who is having one will tell you. Pain in the upper right quadrant radiates to the subscapular region or some other area of the back. It is attended by much lamentation, the sound of which is more impressive than the physical phenomena. The patient may prespire but there are no symptoms of collapse and no graying of the skin. The pulse rate may be increased but the pulse is not running and thready. In the milder cases one may give the patients sedatives by mouth and a hot pack. It is possible that the pain will subside before the sedative given has time to act. If the pain is more severe, the doctor gives subdermically a quarter grain of morphine. If there is a nurse about to administer the drug, it will very likely be prescribed. At any rate the pain subsides and soon the patient is ready to do what she has in mind, albeit with some residual soreness.

If in the futile attempt to expel the offending stone the wall of the gallbladder becomes inflamed and a fibrinous exudate forms on its surface, the great omentum is attracted and by augmenting the size of the distended organ a palpable tumor is produced sensitive to the touch and accompanied by muscular rigidity. If the patient has the leisure and has the services of a nurse, this period is considerably important. Hot packs should be applied and bed rest on her back should be prescribed. The laboratory is set in motion, *x*-rays are made which, if done capably, will show the number and size of the stones. The condition now enters the scientific stage and the patient may be said to be having adequate medical care. On the other hand, if the patient is neither poor enough nor rich enough to command such services and has a flock of children to get off to school, she usually manages to get about for a few days until the pain subsides. She does not have adequate care because the doctor does not know the size and the number of the stones.

If the regression does not take place in a few days, one of two processes may supervene: The inflammation may subside but the obstruction to the cystic duct may remain and the gallbladder becomes distended because its contents cannot escape. We then have a hydrops of the gallbladder. This is signalized by subsidence of the muscular rigidity while a rounded tumor remains. These tumors may become very

large. I have seen one drained by an incision just above Poupart's ligament under a mistaken diagnosis by an eminent surgeon. I saw one which extended into the pelvis and was mistaken for an ovarian cyst.

On the other hand, the gallbladder remains large, the muscular rigidity continues and the tenderness increases. The patient is bedfast, and if this continues beyond four days, the possibility of involvement of the gallbladder wall comes into question. It may be seeping bile because of a local necrosis of the wall, which by flowing over the watershed of the great omentum may overshadow the original lesion and an appendiceal abscess be diagnosed. Or an abscess may form on the surface which, if the omentum be active enough, encloses it and the process remains local. It may cease to be local and the abscess escape the vigilance of the omentum and a spreading peritonitis results.

If the lesion increases after the fourth day, the surgeon can see more clearly what is going on. The process now reverts from scientific medicine and becomes the problem of the practiced surgeon. If a walled-in abscess is found, the prudent surgeon will insert a drain and quit. If there is no abscess but a necrotic gallbladder, a drainage of the organ itself is imperative, and the operator must be careful not to loosen any of the protective adhesions. The stones may be left undisturbed. If there is neither abscess nor necrosis, merely a much thickened gallbladder wall with omental adhesions, the desire to remove the offending organ is tempting in inverse proportion to the experience of the surgeon. It seems logical to remove the organ and be done with it. Ofttimes the conservative surgeon attempts to remove the gallstones, leaving the organ for a later stage. He finds the stones in the cystic duct so imbedded by the edematous wall that they cannot be removed and he reluctantly decides to remove the gallbladder. Technically, the operation by an experienced operator offers few difficulties. The cystic duct and all the region about is much thickened by edema but the surgeon is able to find his landmarks and the operation is concluded.

Here lies the devil's most perfect handiwork. The cystic vessels share naturally the edema of the tissue in which they lie. This means that after ligation a fibrinous clot cannot form, that there is but an inert mass incapable of uniting with the vessel wall and that in about a week it loosens, goes on its way and a lung embolus develops. Such accidents are not common but it is one of the most potent causes for the surgeon to long for the day when he can retire. If one must operate in such conditions, the cystic duct is ligated near the common duct but the vessels are followed upward as far as possible before they are ligated. This gives a longer plug which, theoretically at least, should be less likely to break loose.

The most severe gallbladder affection is gangrene. It is exactly like the affection of the appendix. There is an initial very severe pain, the cry of dying tissue resulting from occlusion of the cystic artery causing total death of the entire gallbladder. This may follow any of the stages noted above. After the severe initial pain of about twelve hours it ceases. The gallbladder being dead, it causes no more pain. If adhesions have not yet formed, they will not do so now. If already formed, they will loosen.

The pain having ceased, the patient likely will say she is free from pain and that she feels quite well. The pulse rate may be normal but the pulse is jerky, even like the surgeon's. The patient is interested in the ceiling while saying she feels all right. The patient has a peculiar gray tinge; she looks as if her hemoglobin is about 40 but the laboratory reports 75 per cent or more.

Better have a look at once for in about four days the living tissue separates from the dead tissue and the entire gallbladder contents escape into the more or less free peritoneal cavity. Then it is too late. Fortunately, these disasters like pulmonary embolism are rare even in the busy surgeon's practice but even one is too many. But few surgeons know the difference between necrosis and gangrene and here is the place to learn.

Arthur E. Hertzler, M.D.

Original Articles

THE PRECANCEROUS MOUTH LESIONS OF AVITAMINOSIS B*

THEIR ETIOLOGY, RESPONSE TO THERAPY AND RELATIONSHIP TO INTRA-ORAL CANCER

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THE purpose of this report is first, to call attention to the capacity of avitaminosis B to cause irritative and precancerous lesions of the oral mucous membranes; second, to describe the nature of such dietary deficiencies and the frequency with which they occur; and third, to evaluate the significance of avitaminosis B in the etiology and in the treatment of intra-oral cancer.

We shall attempt to demonstrate that degenerative and precancerous changes in the oral mucous membranes are among the important symptoms of deficiency disease, and also that avitaminosis B is the greatest single cause of such precancerous mouth lesions. In a review of the literature we have found no reference to the rôle of avitaminosis B in the etiology of mouth cancer.

We have endeavored to substantiate statistically all opinions and conclusions here expressed, but where such proof is not obtainable, we have depended upon the circumstantial evidence drawn from the clinical observations and the cumulative experience of the staff of the Head and Neck Clinic at Memorial Hospital, where about 400 new cases† of mouth and pharyngeal cancer are seen annually. All patients are re-examined regularly in the observation clinic as long as they survive, so that at the present time, there are about 1,500 active cases of mouth cancer being followed in the clinic and private offices of the staff.

In order to obtain specific data regarding dietary deficiencies, three parallel series of 100 cases each (I—precancerous stomatitis, II—mouth cancer, III—normal controls) were selected at random from the clinic, as will be discussed in further detail.

NATURE AND SIGNIFICANCE OF PRECANCEROUS LESIONS IN THE ORAL MUCOUS MEMBRANES

In most cases of intra-oral cancer, there are in addition to the primary lesions, definite degenerative changes in the oral mucous membranes which obviously have antedated the malignant growth. It has long been noted that such degenerative tissue changes are found in a majority of patients with mouth cancer, and, therefore, they are commonly referred to as *precancerous*.** These degenerative and precancerous

† This figure is to the exclusion of cancer of the skin, soft parts and bone of the head and neck and cancer of the nasal cavities, nasopharynx, paranasal sinuses, salivary glands, intrinsic larynx, thyroid, eye and orbit, which collectively comprise about 1,000 cases yearly.

** The terms, *precancerous* and *precancer*, refer to any lesion or morbid state which commonly precedes the

* This investigation was added by a grant from Fleischmann Laboratories, New York. From the Head and Neck Service of Memorial Hospital, New York City.

changes are clearly due to some form of mild injury, persisting for a long time, in other words, to chronic irritation.

It was formerly believed that such degenerative changes were always produced by some local irritant acting within the mouth, and it is only in recent years that the existence of an intrinsic factor has been recognized; that is to say, that these lesions can be produced by a deficiency of certain essential vitamins. Thus far, clinical evidence has indicated that in this country the main dietary cause of such precancerous lesions in the oral mucous membranes is a deficiency of the vitamin B complex. There is little to show that any other vitamin except B is an important factor in this regard.

The degenerative changes which have come to be recognized as precancerous in the oral mucous membranes are: leukoplakia, subacute or chronic inflammation, vascular injection, atrophy or hypertrophy of the papillae, erosion of the epithelium, etc. Most of these can be produced by any of the various forms of chronic irritation such as tobacco, syphilis, dental trauma or sepsis.

Although in practically all clinical reports on intra-oral cancer it is accepted as a fact that chronic irritation plays an important etiologic rôle, nevertheless, opinion is not uniform as to the most responsible form of irritant and it is often implied that a single irritant (tobacco, syphilis, dental trauma, etc.) acting independently can frequently be the sole cause of cancer. Some authors stress the importance of tobacco, others syphilis, still others, sepsis, and the classic belief, dating from the days of Hippocrates, is in the singular importance of the trauma of sharp teeth. The perspective here is too narrow. In the average case the presence of more than one irritant can be demonstrated. Since the reactions of the oral mucosa to the various irritants are so similar, it is not always possible to determine their relative etiologic significance except by therapeutic tests.

While it is probable that in most cases the cancerigenic response of the mucous membranes is due to the combined action of several factors, nevertheless, a single form of irritant may be so pronounced in a certain instance that it can be held mainly responsible; as for example, syphilis in a patient with other demonstrable lesions of that disease and positive serological tests, but with no history of smoking and no signs of a dietary deficiency. The same can sometimes be demonstrated with avitaminosis B or with overindulgence in tobacco.

Finally, the significance of a given form of irritation can depend on its chronicity and prevalence among the population as a whole, rather than on its unique cancerigenic capacity. In this respect it is probable that the stomatitis of avitaminosis B outranks all other forms of chronic irritation.

THEORETICAL RÔLE OF THE VITAMIN B COMPLEX IN THE ETIOLOGY AND SYMPTOMATOLOGY OF MOUTH CANCER

At least three apparently unrelated types of clinical observations can be adduced in support of the theoretical rôle of the B complex in the etiology and symptomatology of mouth cancer: the vitamin deficiency natures of (1) cancer cachexia, (2) radiation sickness, and (3) precancerous stomatitis of obscure origin.

Cancer Cachexia. In the Head and Neck Clinic at Memorial Hospital, our first intimation of the rôle played by dietary deficiencies in mouth cancer came about ten years ago, when we found that our unsuccessful attempts to relieve malnutrition in patients under treatment for intra-oral cancer (especially those in the advanced stages of the disease) were often not due to an insufficient caloric intake alone but also to the nature of the diet in

development of a malignant growth. It should be clearly understood that a *precancerous* lesion is not the "cause" of cancer, but rather that *precancer* is a prodromal stage or prodromal symptom which indicates that the chance of developing cancer is far greater in a given case or at a given site than in the normal. In other words, precancer and cancer have at least some etiologic factors in common.

other respects. We found that while malnutrition was not always relieved by a high caloric diet composed of milk, raw eggs, butter, lactose, etc., the addition to this diet of a few ounces of pureed green vegetables often brought about an immediate and steady gain in weight and an improvement in the sense of well-being. For several years we continued such a dietary régime empirically, not realizing that these beneficial effects were probably mainly due to the correction of a vitamin deficiency.

Radiation Sickness. Not long after Minot, Cohn et al.[26] demonstrated that pernicious anemia could be relieved by the administration of liver concentrates, it was discovered that the so-called "radiation sickness" (malnutrition, mental depression and asthenia) associated with fractionated radiation therapy could also be markedly relieved by the administration of liver concentrates. The value of this empiric measure was noted independently by several investigators (Dietel,[8] Young,[41] Webster[38]) and was widely discussed among cancer therapists.

The concept of what constitutes "radiation sickness" has undergone considerable change during the past twenty-five years. The term was originally used to designate a symptom complex consisting of headache, nausea, malaise, which followed immediately after the administration of the long (twenty minutes to one hour) *x*-ray treatments which were necessary with the *x*-ray machines available a quarter of a century ago.* These symptoms were formerly believed to be due to the disagreeable odor and toxic effects of the ozone generated in the electrical fields of the exposed high tension aerials.

By about 1930, the earlier causes of radiation sickness had been largely eliminated, and at this time the practice of daily fractionation in *x*-ray therapy was introduced and the concept of radiation sickness changed. Instead of transitory nausea and headache immediately following a treatment, there occurred a different type of disability, consisting of anorexia, progressive malnutrition, asthenia, mental depression, which came on, or at least was markedly aggravated about two or three weeks after the institution of the fractionated therapy. This symptom complex then came to be known as radiation sickness and it was found that the administration of liver extract was usually followed by a noticeable improvement. When viewed with broad perspective, it is entirely reasonable to explain the latter form of radiation sickness as an acute vitamin deficiency, brought on by progressive restriction of the diet, incident to the radiation reaction, and superimposed upon other debilitating effects of the malignant tumor, such as pain and sepsis. The same syndrome, when not so clearly associated with radiation, has long been known as "cancer cachexia." In brief, radiation sickness refers to a condition which existed previous to, and is only indirectly related to radiation therapy, although aggravated by it.

Precancerous Stomatitis of Obscure Origin. About 1933, C. P. Rhoads, then of the Rockefeller Institute, during the course of his investigation on the etiology of certain disorders of the oral mucous membranes,

* The therapeutic *x*-ray machines available during the second decade and the early part of the third decade of this century always necessitated exposed high tension aerials in the treatment room. These high tension aerials were not insulated from the air, or "shock-proofed," as in the present day apparatus and during the operation of the machine, electrical fields were produced in the air, especially opposite all sharp points. The electrical fields or coronas were evidenced by the presence of sparks and crackling noises. Within these electrical fields the air was ionized with the formation of ozone and oxides of nitrogen. These ionization products possessed a disagreeable odor, especially pronounced at the end of a long treatment period. Many patients complained of the odor and believed that their distressing symptoms were due to this cause. Some measure of relief was obtained by providing more adequate ventilation in the treatment room. The syndrome of headache, nausea, etc., was probably due to a combination of causes: the effect of inhalation of the ionization products, the disturbing influence of the crackling noises and emotional stress. By about 1930 the improvement in design of *x*-ray apparatus included almost complete elimination of exposed high tension aerials, which by then had been shock-proofed. As a result, the above noted causes of radiation sickness were largely eliminated.

included in his clinical material a number of patients from our clinic, with precancerous lesions of the mouth.* He demonstrated to us that in many instances such precancerous lesions improved and sometimes disappeared completely under the administration of an adequate quantity of some crude preparation rich in the vitamin B complex. During the investigation it was shown that the most dependable source of the B complex was dried granular brewer's yeast, taken by mouth.

Preliminary Conclusions. The strong presumptive evidence of the observations just described lead us to begin the routine administration of vitamin B usually in the form of brewer's yeast,† to all patients under treatment for intra-oral cancer. The results of such a routine were so gratifying that although there are as yet no methods available for obtaining absolute statistical proof, we nevertheless concluded empirically that the abnormal changes in the oral mucosa resulting from avitaminosis B are undoubtedly more prevalent and of more importance in the etiology of mouth cancer than any other single form of chronic irritation and possibly of greater significance than the sum total of all other etiological factors.

We believed, therefore, that a survey of the dietary habits of patients with precancerous changes in the mouth, and also of those with intra-oral cancer, might reveal a high percentage of diets which were inadequate in vitamin B. We consequently undertook a systematic investigation of the diets of three parallel series from our clinic: Series I: 100 patients with precancerous stomatitis; Series II: 100 patients with fully developed mouth cancer; Series III: 100 normal controls (patients or their relatives) without any demonstrable complaint or lesion in the oral cavity.

An analysis of the dietary histories in these groups supported our theories in fact although not to the degree which we had expected. Nevertheless, the beneficial effects of vitamin therapy are incontestable in a large percentage of patients with intra-oral cancer or precancer, even though in some of them no deficiency can be demonstrated by the dietary histories or by any laboratory test thus far devised.

NATURE OF THE VITAMIN B COMPLEX

In the early days of vitamin research, vitamin B was thought to be a single substance, but later investigation has revealed that the B complex consists of from seven to twelve separate fractions which occur in association in foods in the natural state. The best known vitamin B fractions are B_1 (thiamin), B_2 (riboflavin), P-P (nicotinic acid), B_6 (pyridoxin), and pantothenic acid. Other components thought to be a part of the B complex are B_3, B_4, B_5, factors L_1, L_2, U, vitamin M, para-aminobenzoic acid, the antigray hair factor and choline. The respective rôles of all of these substances in the maintenance of health in human beings have not been determined as yet; investigations on the more recently discovered fractions have been confined largely to animal

* The concept of inflammatory, ulcerative and atrophic lesions of the oral mucous membranes as a manifestation of a dietary deficiency, dates from the early studies of Manson[22] on tropical sprue. Later Goldberger[13] proved that in both man and animals the oral lesions of pellagra could be caused by a lack of some heat stable constituent of yeast and could be cured by supplementing the deficient diet with the missing factor. In a study of chronic canine black tongue, a deficiency disease of dogs, etiologically and symptomatically like pellagra in man, Rhoads and Miller[32] produced marked atrophic and inflammatory glossitis. The lesions disappeared promptly after a good source of vitamin B (yeast, or liver extract) was added to the deficient diet.

In 1932, Castle and Rhoads[5] published a preliminary report of an extensive study of tropical sprue in which the changes of the oral mucous membranes were used as an index of effective treatment. Later these same authors in a complete report presented evidence that the stomatitis of sprue, pellagra, and pernicious anemia are manifestations of a dietary deficiency of some constituent, similar in distribution to the heat stable vitamin B complex.

This thesis was supported by the work of Oatway and Middleton[30] and of Hutter, Middleton and Steenbock,[15] in which further experimental and clinical evidence was advanced to substantiate the view that one group at least, of inflammatory and atrophic lesions of the mouth were caused by a vitamin B deficiency and were curable by foodstuffs rich in that complex. The lingual manifestations of nutritional deficiency are illustrated in a publication by Minot and Castle.[25]

† We have employed for this purpose, Fleischmann's Dried Granular Brewer's Yeast, No. 2040.

experiments. In Table I are listed the known functions of the B components, the symptoms of their deficiencies, and the average minimum daily requirement in healthy adults. It should be noted that these minimal amounts for normal persons are far below the therapeutic dosage necessary in well established cases of vitamin deficiencies. The reasons for this apparent discrepancy will be discussed later.

riboflavin are leafy green vegetables such as kale, spinach, turnip greens, carrot tops and beet tops, dried prunes, cheese and milk. Nicotinic acid is provided in lean meat and poultry, leafy green vegetables, milk, tomatoes and wheat germ. Pyridoxin is found in raw egg yolk, butter, nuts and cheese. The B complex does not occur in standard quantities in natural foods. Two different crops of the same vegetable may

TABLE I

THE VITAMIN B COMPLEX

Factor	Function	Symptoms of Deficiency in Man	Average Minimum Daily Requirement for Adult
B_1 (thiamin)	Concerned with carbohydrate metabolism	Polyneuritis	1 mg. (300 I.U.)
B_2 (riboflavin)	Maintains integrity of the oral mucous membranes	Cheilosis, perleche, lesions at corners of mouth, eyes, and nose	2 mg.
P-P (nicotinic acid)	Maintains integrity of nerve function, concerned in skin and oral mucous membrane nutrition	Pellagra—dermatitis, stomatitis, gastrointestinal disturbance, dementia	10 to 20 mg.
B_6 (pyridoxin)	Fatty acid metabolism? Maintains integrity of myoneural junctions? Prevents acrodynia dermatitis in rats	Nervousness, insomnia, difficulty in walking, myotonia?	Not known
Pantothenic acid	Prevents dermatitis in chicks	Not known	Not known
B_3 (Williams-Waterman factor)	Concerned with bird weight maintenance	Not known	Not known
B_4 (Reader factor)	Rat paralysis preventative	Not known	Not known
B_5 (Peters factor)	Concerned with pigeon weight maintenance	Not known	Not known
Factors L_1 and L_2	Lactation factors for rats	Not known	Not known
Factor U	Growth factor for chicks	Not known	Not known
Vitamin M	Prevents nutritional cytopenia in monkeys	Not known	Not known
Antigray hair factor	Prevents gray hair in rats	Not known	Not known
Para-aminobenzoic acid	Concerned with bacterial metabolism	Not known	Not known
Choline	Prevents fatty liver in rats and dogs, perosis in chicks, and focal hemorrhages in the kidney of rats	Not known	Not known

Although liver and yeast are the outstanding sources of the vitamin B complex as a whole, other foods contain varying amounts of the separate B fractions. For instance, good sources of thiamin other than yeast and liver are lean pork, soy, lima and kidney beans, nuts, whole grains and egg yolk, while the best sources of

contain varying amounts of thiamin, riboflavin, nicotinic acid, etc. In addition, methods of processing and of cooking affect the fractions in different ways.

The daily minimum requirement of each of the B components for individuals is dependent upon several factors. It is known that since thiamin is related to carbo-

hydrate metabolism, persons whose diets are composed largely of carbohydrates will require greater amounts of thiamin. The need for this fraction is also increased directly with body weight.

Since the several B fractions occur in such close association, a proved deficiency in one is strong presumptive evidence of a deficiency in all the others although the symptoms may differ in character and degree. Some investigators have found that in certain sections of the country, because of dietary habits or unavailability of certain foods, there is more evidence of a deficiency in one factor of the complex than in the others, and that the administration of a crystalline form of this one factor will give fairly successful therapeutic results. This is particularly true in the pellagra districts of the South where nicotinic acid has been found to relieve most of the neuropsychiatric and dermatologic symptoms of the disease. In the northeastern states, however, the symptoms and signs of a deficiency which in many respects resembles pellagra, have, in our experience, never been relieved by nicotinic acid alone. Satisfactory results among our patients have been obtained only by administering some crude preparation like brewer's yeast, which contains in its residue, after isolation of the known components, some unknown or not clearly identified factors which are apparently essential to good health.

SIGNS AND SYMPTOMS OF AVITAMINOSIS B

The abnormal changes which result from an inadequate intake of the vitamin B complex are both objective and subjective. The sites and characteristics of the local signs and general symptoms may vary widely. Such variations could be due to differences in the individual's reaction to deficiencies of a given B fraction, or to differences in an individual's requirement of a given fraction, or to differences in the make-up of deficient diets. The variation in symptoms could also be explained, at least in part, by a synergistic action of the B components, assuming that an absence of one interferes with the effect of the others. It is plain that the mental depression of a thiamin deficiency would naturally be accompanied by a loss of appetite and a lowered general state of health, which in turn would interfere with the absorption and metabolism of all ingested vitamins. Similarly, an inadequate intake of riboflavin with the characteristic mucous membrane lesions would result in a loss of appetite and, therefore, a diminished diet and vitamin intake.

Characteristic symptoms of an insufficiency in a single fraction can be produced with fair regularity in human beings, but such specific deficiencies can never occur spontaneously, since the several factors of the B complex are always associated in foods in the natural state. Because of such overlapping of the various causes and effects, no particular attempt will be made in the following discussion to identify the specific component of the B complex directly responsible for each symptom. The symptomatology in general will be considered as it applies to the problem of intra-oral cancer.

General Symptoms. In the taking of histories, it is often difficult to elicit from the patient such symptoms as constipation, anorexia, asthenia, dermatoses, onychodystrophy, mucous membrane changes and psychoneuroses, when present in mild degree, since he often does not recognize their existence until they have been relieved under treatment. In many published reports there has been a tendency to overlook the causal relationship and the full significance of such apparently unrelated symptoms as insomnia, malnutrition, stomatitis, etc. When considered from the standpoint of the specialist (dermatologist, psychiatrist, nutrition expert, cancer surgeon, etc.) the importance of a certain group of symptoms may be properly emphasized to the partial exclusion of the others. In this connection, we acknowledge that in the present report we are concerned mainly with the lesions in the oral mucous

membranes and their relation to precancer and cancer.

Malnutrition. One of the most common but by no means constant objective symptoms of vitamin B deficiency is malnutrition. This disorder is probably due to a combination of causes, anorexia and a lessened food intake with a decreased metabolism of carbohydrates as well as a general lowering of the state of health. Some patients may exhibit practically all of the symptoms of avitaminosis B (mental depression, stomatitis, dermatoses, etc.) associated with moderate or slight overweight. On the other hand, one of the most striking responses to vitamin B therapy is weight gain. (In Series I, or the stomatitis group, referred to in this report, there was some weight gain in forty-nine patients—51 per cent—the average gain was twenty-five pounds, the greatest gain in any individual being thirty-nine pounds.) When malnutrition is present in avitaminosis B, it tends to be marked and progressive.

It is erroneous to assume that malnutrition in patients with mouth cancer is due only to the difficulty and discomfort in taking food. While these obstacles play a prominent rôle, nevertheless, forced feeding to the point of tolerance, by mouth or by nasal tube, of from 3,500 to 4,000 balanced calories a day will often have little effect on a patient's weight unless provision is made for an adequate vitamin intake. For this reason, such diets should contain generous amounts of purees of green vegetables, supplemented by either natural vitamin B concentrates such as yeast or liver or synthetic preparations.

It is doubtful whether any exact standards can be set up for correlating the proper body weight with any combination of height, age and sex, although tables of such averages have been approximated which are useful in physical education. It is common observation, however, that marked variations from the average state of nutrition are compatible with good health and that such departures from the norm are often found in persons who possess to an unusual degree, such qualities as physical and mental vigor and longevity. While leanness often seems to favor a long life, nevertheless, malnutrition constitutes a definite hazard when associated with a long and debilitating illness such as cancer.

Neuropsychiatric Symptoms. All investigators have noted the frequency of nervous and mental disorders as a part of the symptom complex in avitaminosis B. Jolliffe[17] has recently discussed this subject in considerable detail. In this connection it is of interest to mention the experiment of Williams and Mason.[40] They obtained eleven female volunteers, who agreed to live in the hospital on an accurately measured and controlled diet, which was normal in all respects except that it was inadequate in thiamin. The subjects for this experiment were selected because of their willingness to co-operate, their previous satisfactory diets and the absence of any marked physical or emotional abnormalities. After a few weeks on this inadequate diet, all the previously normal volunteers became depressed, irritable, quarrelsome, and unco-operative, and developed other personality changes. These neuropsychiatric symptoms progressed to such a degree that finally open rebellion against the routine was threatened. The disturbance was immediately relieved and the subjects returned to normal when adequate thiamin was added to the diets.

The practical analogy between this experiment and the management of an apprehensive and nonco-operative cancer patient should be obvious. To the less intelligent person, a diagnosis of cancer is often equivalent to a death sentence, and even the best informed knows that with the exception of superficial cancer (such as cancer of the skin and lip), the over-all cure rate is not as high as 50 per cent, in other words, there is not an even chance for survival. Such melancholic speculations in themselves naturally tend to produce mental depression, but the despondent mental state in patients with mouth cancer is not necessarily due solely to such morbid

reflections. If avitaminosis B is present in most cases as a precancerous condition, then the worry and apprehension accompanying the knowledge, or the suspicion of cancer, would be superimposed upon a pre-existing mental depression caused by a long-standing vitamin B deficiency.

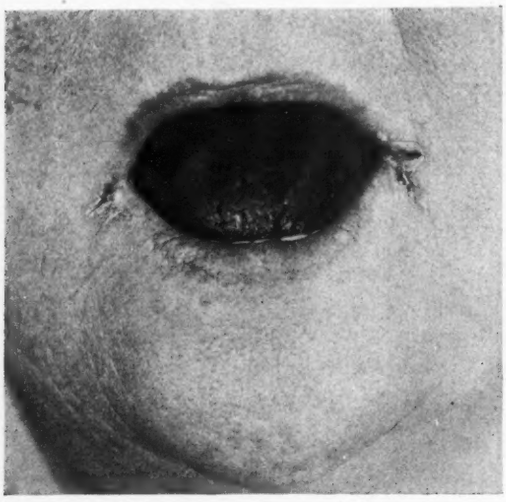


FIG. 1. *Perleche* in a female, aged sixty-two, who had complained of crusting and fissuring at the labial commissures for a period of one month. There was also a marked degree of hypertrophy and agglutination of the papillae, and fissure folding of the mucosa of the tongue (scrotal tongue).

One of the common accompaniments of mental depression is cancerphobia, which causes great distress to those so afflicted. The tendency of such harassed individuals to seek medical advice for such lesions as are definitely precancerous is obviously salutary. On the other hand, many neurotic patients complain bitterly of painful or burning sensations in the tongue but show no objective signs of abnormality. Although most of these probably suffer from avitaminosis B, the underlying nature of the disorder is not often recognized; and because of their repeated complaints, they constitute minor nuisances to their families and associates. A typical example of such a symptom complex is the following case report:

CASE 1. M. J., a male dentist, aged thirty-seven, applied in March, 1940, for advice concerning a "sore" tongue of several months' duration, which he feared to be cancerous. He slept poorly and worried a great deal, and he ascribed these ner ous symptoms to marital discord which had progressed to the point where he considered a divorce the only solution. Objectively, there were only moderate changes in the tongue. The papillae were slightly hypertrophied and there was some lessening of the normal furring at the borders of the tongue. In a casual examination, with no complaint on the part of the patient, such a tongue would probably have been passed as normal.

The patient was assured that he had no sign of cancer, the probable nature of his disorder was explained, and he was advised to take large quantities of green vegetables and three tablespoonfuls of dried granular yeast daily. Two weeks later he returned for re-examination in a much more cheerful frame of mind. There was moderate improvement in the appearance of his tongue. He had gained five pounds, his bowels moved twice a day, and he had come to realize that previously he had been constipated. Guarded inquiries regarding his marital difficulties brought forth the rather embarrassed statement that since the improvement in his "disposition," these troubles had completely disappeared. He was advised to continue the vitamin therapy and corrected diet. When seen again after a few months, there had been no recurrence of the mental or oral symptoms.

Perleche, Cheilosis and Generalized Dermatosis. As first described by Sebrell and Butler,[34] one of the objective symptoms of a deficiency of the vitamin B complex, is a scaly, crusted, fissured erythema at the labial commissures (Fig. 1), sometimes extending for a short distance onto the vermillion border of the lips (cheilosis). This symptom, as well as the attendant mucous membrane changes, is thought by some observers to be the result of a deficiency in riboflavin, although Goldberger,[13] Jolliffe,[16] Manson-Bahr,[23] Drazin,[9] and others, consider a lack of nicotinic acid to be the important factor. It seems doubtful to us that the explanation of this lesion is so simple, since in a few instances we have observed perleche to develop first and to persist in patients who were receiving

massive doses of riboflavin (20 mg. daily) as part of their treatment for deficiency stomatitis. Such observations suggest that caution is necessary in attributing any specific lesion or symptom to a deficiency in a single fraction of the vitamin B complex. In our experience, neither perleche nor any other single symptom has responded as well to the administration of a particular B factor, as to a combination of several components or to such natural concentrates as yeast or liver.

Cheilosis often appears to include a disorder of the mucous and minor salivary glands of the lip, characterized by a sticky viscid secretion which, when dried, forms a brownish line on the lips. In aggravated cases, the mucous membrane has a finely mottled appearance marking the duct openings of the inflamed glands. In our experience, neither perleche nor cheilosis are precancerous lesions in themselves, but they usually indicate the presence of other degenerative changes within the mouth on the tongue or cheeks, which at these sites are precancerous.

In some instances a dermatosis of the same origin is more widespread, affecting the skin about the alae of the nose, the ears, the cheeks, the dorsum of the hands and fingers, or even the entire body. In pellagrins, dermatoses are a characteristic symptom, beginning first, according to Spies, Hightower and Hubbard[35] as an erythematous area somewhat resembling sunburn which later changes to reddish brown. After desquamation, the skin seems to be abnormally red and thickened and permanent pigmentation may develop following frequent recurrences of the dermatitis.

Onychoclasis, Fragilitas Unguium and Onychodystrophy. Fragility and dystrophy on the fingernails are among the earliest and most common dermatologic manifestations of a vitamin B deficiency. The patient is sometimes unaware of these disorders until they begin to improve under specific therapy, as is also the case in the subclinical symptoms of constipation, anorexia and asthenia of deficiency disease. It is significant that in a large percentage of patients with obvious mouth lesions of avitaminosis, guarded inquiries concerning the condition of the fingernails will elicit an admission that the nails tend to break easily (onychoclasis, fragilitas unguium). Other patients will insist that the nails and hair grow faster after vitamin B therapy.

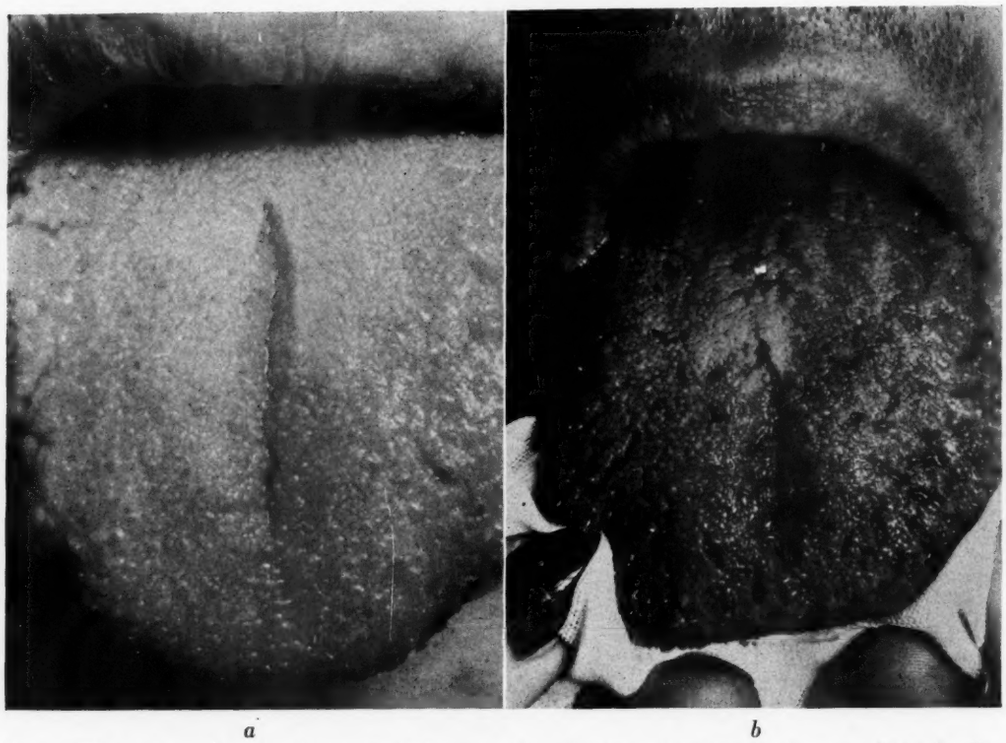
Objectively, in cases of mild vitamin B deficiency, the nails may present longitudinal reeding, while in marked avitaminosis, onychodystrophy may appear in the form of transverse corrugations indicating variations in the rate of nail growth. From the practical standpoint, when there is some question as to the origin of mild disorders of the mucous membranes and/or malnutrition and asthenia, these abnormalities of the fingernails are of value as corroborative signs in the differential diagnosis of avitaminosis.

Oral and Pharyngeal Symptoms. In addition to the general and systemic symptoms already mentioned, there are inflammatory and degenerative changes of the oral and pharyngeal mucous membranes which are among the most common and most important manifestations of avitaminosis B. These degenerative changes are the result of subacute and chronic inflammation. There are several forms and combinations of these mucous membrane lesions, the particular variations probably depending upon the time intensity ratio, that is, slight deficiencies existing over a long period of time would undoubtedly produce different types of lesions (atrophy, leukoplakia, etc.) from severe acute deficiencies existing over shorter periods (acute inflammation, ulceration). In a few cases, we have been able to observe the progressive development of such degenerative changes in previously normal oral mucous membranes. (Fig. 2.)

Prior to the more recent discoveries in deficiency diseases, Oatway and Middleton[30] reported the occurrence of abnormalities of the tongue and mouth, in a variety of disorders including hypo- and hyperchlorhydria, gastric ulcer and cancer. Most of the mouth lesions which they describe

can be explained on the basis of an underlying or associated avitaminosis B. Spies, Hightower and Hubbard[35] and Rhoads and

inflammation or of the ulceration which is sometimes found in acute vitamin B deficiencies.



a *b*

FIG. 2. The progressive development of degenerative changes of avitaminosis B resulting finally in scrotal tongue. S. G., male, aged thirty-two, was first seen in November, 1933, complaining of mild burning sensations in the tongue. The nature of the disorder was not recognized and there were no definite lesions observed in the tongue. The symptoms continued and a few months later mild inflammation and hypertrophy of the papillae were noted. *a*, The condition was then recognized as probably being due to a dietary deficiency and he was placed on vitamin therapy.

The patient was then lost to observation for a period of eight years after which he returned with aggravated symptoms (sore tongue, loss of weight, asthenia, mental depression). Neuropsychiatric symptoms were such that he had become emotionally unstable and burst into tears during the interview. Marked progressive changes had occurred (scrotal tongue). *b*, He was directed to take 45 Gm. of granular yeast daily, and within a month he had gained about ten pounds in weight. The asthenia, mental depression and subjective symptoms in the tongue had completely disappeared.

Miller[32] have described in considerable detail the oral mucous membrane changes which accompany this form of deficiency disease.

Glossodynia. The chief subjective symptom in the mouth in avitaminosis B is pain, a burning sensation, or soreness of the tongue and sometimes of the cheeks or gums. Some patients complain of a constant dull pain chiefly in the tongue while the organ is at rest. Others find that hot or acid foods cause local discomfort. This hyperesthesia is a natural consequence of

In milder chronic avitaminosis B, pain or burning of the tongue may be a prominent symptom with little or no evidence of any mucosal abnormality. For this complaint the term *glossodynia* has long been used. Although it has been suspected that the condition was due to more than one cause, it has remained one of the minor unsolved medical problems. Some investigators have doubted that glossodynia represents a disease *sui generis*, and as Fox[12] found in his series, most of the patients are "chronic worriers." It is now obvious that most of

these cases are due to avitaminosis and that the symptoms can be completely relieved by vitamin therapy. From the point of view of cancer diagnosis, it is significant that one of the aggravating factors in almost all cases of glossodynia is an associated cancerphobia.

Inflammatory Hyperemia of the Mucous Membranes. The basic response of the oral mucosa to a vitamin deficiency is chronic inflammation which closely resembles in appearance that produced by toxic, chemical, bacterial, traumatic or thermal agents. Although in a vitamin deficiency, there is no sound theoretical basis for assuming the existence of an irritant, we shall nevertheless use the terms *irritant, irritation* and *inflammation* in discussing mucous membrane lesions of avitaminosis, since we know of no better term to describe this disorder.

In severe and protracted vitamin B deficiencies, the affected membranes—most often of the tongue, and sometimes of the cheeks, gums, and palate—are deeply injected and inflamed, and often tender or even painful. This lesion may be asymmetrical or almost unilateral in the cheek and palate. In acute cases the appearance of this inflammation in the tongue may be obscured by furring. In severe and prolonged cases there is usually a disappearance of the normal coating or furring with some degree of papillary atrophy, and the mucosa of the tongue may have a diffuse reddish tint as if stained by a dye. In moderate degrees of deficiency, the inflammation and/or the disappearance of furring may occur only at the borders and on the tip of the tongue.

Inflammatory hyperemia of the tongue, cheeks or gums in avitaminosis B is one of the most significant precancerous lesions because it indicates the presence of a marked degree of chronic inflammation. It is found in association with atrophy of the papillae and cancer more often than any other degenerative change.

Ulceration. This symptom usually occurs only in the acute or exacerbated stages of the aforementioned inflammatory lesions. The ulcers may be either single or multiple, they lack specific features and are commonly situated on the edges of the tongue, less often on the cheeks and gums, and have a yellowish irregular base with only slight erosion. Their specific nature is proved by their prompt healing and the disappearance of all attendant systemic and nervous symptoms under vitamin B therapy. Acute ulceration of the tongue in deficiency disease is not often of great precancerous significance because its clinical course is seldom of long duration.

The following case report illustrates this syndrome and its response to treatment:

Case II. A. H., a traveling salesman, aged fifty-one, was first seen in April, 1940. He had noted a painful swelling of his tongue six months previous. His physician had diagnosed the lesion as Vincent's ulcer and had treated him by several intravenous injections of neoarsphenamine. This therapy at first produced improvement in the local symptoms but several subsequent attempts were not so successful and relapses and exacerbations occurred. The Wasserman blood tests were negative. About two weeks before admission the tongue became acutely sore with the appearance of several ulcers on the borders. At about the same time the patient developed acute insomnia, nervousness and mental depression. Arsphenamine therapy produced no improvement. Another physician had been called into consultation and the possibility of cancer discussed with the patient and his family.

At the time of the first interview the patient was in a highly emotional and apprehensive state, ostensibly because of the fear of cancer, and he obviously was having difficulty in restraining himself from weeping. He stated that his best weight was 156 pounds; his weight on admission was 148 pounds. This loss he ascribed to the recent increased soreness of his tongue and the consequent difficulty in eating. He admitted that due to the nature of his business as a traveling salesman, his dietary habits had been irregular. He was a moderate user of alcohol and had himself noted that the severity of his symptoms varied directly with the amount of alcohol consumed.

Local examination revealed the tongue to be slightly swollen with a moderate inflammation of the mucosa of the edges of the anterior half.

FIG. 3. *Ulceration* of the tongue in avitaminosis B. (Case 11).

Mainly on the right, but also on the left, there were several localized, superficial, yellowish ulcers surrounded by local swelling. (Fig. 3.) These lesions resembled herpes and varied from 3 to 5 mm. in diameter.

The patient was directed to take one teaspoonful of liver extract powder and one tablespoonful of dried granular yeast three times a day. Within one week, there was complete healing of the ulcers of the tongue and disappearance of subjective symptoms. Two weeks from the beginning of treatment he stated that his general health was much better, that he slept well and was more active in his business than formerly. At this time he weighed 163 pounds (a gain of fifteen pounds) and his appetite had improved to the point where he feared that he ate too much. One year after admission he was still taking three tablespoonfuls of granular yeast a day. He had experienced no return of local or general symptoms and weighed 166 pounds, the total weight gain being eighteen pounds.

Superficial chronic ulceration and erosion of the mucous membrane is often found in association with "bald" tongue, or complete papillary atrophy, and with leukoplakia, as described in the succeeding paragraphs.

Atrophy and Hypertrophy of the Papillae of the Tongue. The frequent association of bald tongue with severe chronic anemia has been noted for at least a century, and in all of the earlier investigations on pernicious anemia, the significance of this symptom has been emphasized. In recent years, the discoveries of the nature and effects of vitamin B deficiency have indicated that so-called pernicious anemia is also a deficiency disease, probably of the B complex, and that the glossitis and papillary atrophy of pernicious anemia is identical in origin with that found in sprue, pellagra and the common forms of precancerous changes in the mouth.

The velvety furred appearance of the normal tongue is due principally to the finer or filiform papillae and, as Middleton[24] and others have pointed out, in cases of atrophy, these filiform papillae are the first to disappear; the most obvious effect being a decrease in the furring and an increase in the solid pink color of the tongue. As these filiform papillae disappear and the inflammation continues, the larger fungiform papillae, fewer in number, become more evident. Gradually they become shorter, and the surface of the mucous membrane is at first finely pebbled, then becomes progressively smoother and finally bald. (Fig. 4.) An almost identical picture of atrophy occurs in chronic syphilitic glossitis. Bald tongue, when found in association with acute inflammatory hyperemia, is one of the most serious precancerous lesions in the mouth.

In some cases, especially in the milder forms of chronic inflammation (associated with avitaminosis, syphilis and particularly tobacco) there is a combination of atrophy

and hypertrophy so that while the papillae are obviously fewer in number, those which remain are increased in length and thickness. This condition produces a decrease in the furring of the tongue and results in a coarser or less velvety surface. In some instances, the hypertrophy is so marked that when the papillae are separated at any point, an apparent fissure 3 to 5 mm. deep runs down to their bases. These greatly hypertrophied papillae may later become agglutinated over irregular patches and the surface of the tongue coarsely pebbled. In such hypertrophic glossitis, the furring may be brownish in color. (Fig. 5.) Hypertrophy of the papillae is less often found in association with cancer than is atrophy.

Many authors speak of a re-growth of the papillae under specific therapy. In our experience, such regeneration takes place only in the early stages when the atrophy is slight or partial. The lesion of advanced or complete atrophy of the papillae is not reversible and although all acute and subacute inflammation may disappear, the tongue remains bald.

Fissure Folding. This lesion which has sometimes been called "scrotal tongue" is the result of swelling of the mucosa and submucosa, and possibly also of the musculature (interstitial glossitis) so that the tongue becomes too large for the closed oral cavity. Consequently, the organ is compressed and the hypertrophied mucosa and submucosa are forced into folds which become evident as deep, nonulcerated fissures when the mouth is opened and the pressure released. The surface of the tongue then presents an irregular striated appearance. (Fig. 5.)

Leukoplakia. The most common oral lesion resulting from one or more forms of mild, long-standing, chronic irritation is leukoplakia. On close examination, some leukoplakia can be demonstrated in about 50 per cent of all males and in about 10 per cent of all females over forty-five years of age. In clear cases of avitaminosis it is usually impossible to state with assurance that an associated leukoplakia has been caused by the deficiency alone, or by a combination of other factors such as smoking, syphilis, etc. The leukoplakic patches may

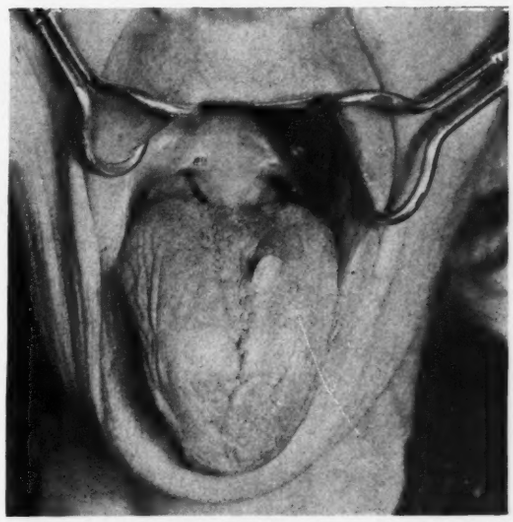
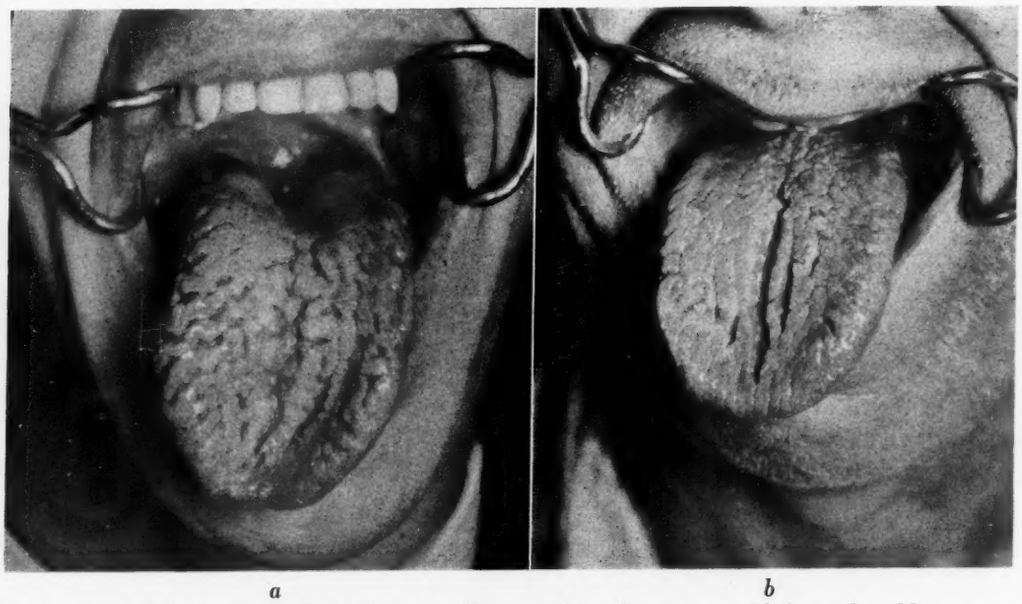


Fig. 4. Complete *papillary atrophy* or bald tongue. B. C., female, aged seventy-nine, with a history of sore tongue of five years' duration. The projection to the left of the midline on the dorsum was removed for histological examination and proved to be benign papilloma.

be small, superficial and present only on the mucosa of the cheeks just back of the labial commissures, or they may be widespread over the mucous membranes of the oral cavity (cheeks, tongue, palate, etc.). When the dorsum of the tongue is affected, there are often irregular thickened patches dispersed on a bald surface. (Fig. 6.) It is this clinical picture to which the term "lingua geographica" is usually applied.

The milder degrees of leukoplakia are of significance from the standpoint of precancer only in that they indicate the existence of chronic irritation. The thickened, fissured, or ulcerated patches of leukoplakia are of more immediate significance in that they may actually be undergoing malignant degeneration. Leukoplakia is not often found in association with the acutely inflamed bald tongue. We have observed cases of patchy striated leukoplakia of the oral mucous membrane associated with dermatoses and previously diagnosed by a dermatologist as lichen planis, which responded to vitamin B therapy.

Gingivitis. The most frequent symptom of a mild gingivitis is bleeding from the gums on brushing the teeth, which of course can occur in any form of gingivitis. Some degree of gingivitis is almost always found in even the mild stages of vitamin deficiency stomatitis. In some aggravated cases the gums are swollen, deeply injected, and tender or painful on mastication. Although the lesion is supposedly more characteristic of avitaminosis C (scurvy), it is probable that the most common cause of



a *b*

FIG. 5. The clinical picture of *scrotal tongue*, illustrated by Figures *5a* and *b*, is produced by a combination of hypertrophy, agglutination of the papillae and fissure folding.

a *b*

FIG. 6. *Leukoplakia.* A mild, long-standing glossitis of avitaminosis, or any other form of irritation, is likely to produce leukoplakia in association with other degenerative changes in the tongue. In this case the patient was a male, aged seventy-two, who had noted white patches on the tongue for a period of fifteen years. *a*, His diet was inadequate and he complained of chronic constipation. He was a heavy smoker, but the Wassermann test was negative. *b*, There was marked improvement under vitamin therapy.

gingivitis, as proved by specific therapy, is a vitamin B deficiency. This lesion is undoubtedly of precancerous significance in gum cancer.

It seems to us that most of the inflammatory lesions grouped under the vaguely defined terms of "trench mouth" and "Vincent's infection" are not primarily bacterial diseases but rather the inflammatory lesions of avitaminosis in which the Vincent's organisms, present in most mouths, are secondary invaders. King[18] has reported the successful treatment of Vincent's infection with nicotinic acid. Williams,[39] in discussing the prevalence of Vincent's angina among Mexican patients, calls attention to the fact that their diets were habitually inadequate in vegetables and fruit, and he believes that the deficiency was mainly one of vitamin C. Topping and Fraser[37] and Tomlinson[36] produced mouth lesions in monkeys varying from a mild gingivitis to complete gangrenous necrosis of the cheeks by feeding the animals diets lacking in the vitamin B complex.

In some cases gingivitis may be the preponderant symptom of avitaminosis B with relatively few or even no objective findings in the tongue or mucosa of the cheeks. In these instances the gingivitis may go on to the formation of bulky granulomas as in the following case report:

Case III. H. C., schoolgirl, aged seventeen, was first seen in March, 1937, with a history of pain and swelling in the left upper gum, of seven month's duration. One month previous to the first interview, several teeth in the left upper jaw became loosened and her dentist discovered a granular tumor in this area. Examination revealed an edematous swelling of the left upper gum, 3 cm. in diameter, extending onto the hard palate. The mucous membrane in the affected region was deeply injected, but not tender, and the rest of the gums were fairly normal. A biopsy was reported as *plasma cell granuloma*. The other clinical and laboratory examinations, including roentograms, were negative.

Under a diagnosis of granulation tissue epulis, the teeth were extracted and the tumor removed locally with curettage and cauterization of the base. Eight months following the operation, the patient reappeared with marked swelling in the subcutaneous tissue of the right cheek and of the right upper and lower gums. Local measures had failed to give relief.

At this time it was suspected that the disorder might be systemic rather than local and therefore she was given liver extract powder, two teaspoonfuls three times a day. In two weeks the gums had practically healed and the swelling in the cheek had disappeared. The liver therapy was continued for several weeks, and then as an experiment, it was stopped and the patient was given nicotinic acid (50 mg. daily). After a few weeks on the latter form of therapy, her gums had again become sore, she had lost fifteen pounds, and her menstrual cycle had become irregular.

She was then placed on vitamin B therapy (Vegex) and within a few days the soreness of the gums had subsided. She soon regained her lost weight and the menses returned to normal. Since that time she has experimented with several forms of vitamin B therapy, under our direction, but she reacts best to liver extract powder. If she stops taking the liver, she immediately begins to lose weight and the gums become sore. It is noteworthy that in this case relief can be obtained only by the use of crude concentrates and not by a single fraction of the B complex such as nicotinic acid.

Salivary Changes. In severe prolonged deficiencies of the B complex, the mucous membranes of the mouth appear to be drier than normal with a loss of normal gloss and with a brownish tint in the furring of the dorsum of the tongue. The saliva is lessened in quantity and increased in viscidity. The cause of this abnormality may be, in part, a decrease in the volume of saliva secreted by the parotid and submaxillary salivary glands as the result of malnutrition, lack of appetite and decreased fluid intake. It is probable, however, that this symptom is due also to a disorder of the minor salivary and mucous glands, which are numerous in all of the oral mucous membranes and whose secretions lubricate and moisten the mucosa. One of the most characteristic responses to vitamin B therapy is the disappearance of the brownish color in the mucous membranes and the resumption of

their usual pale, pink, glistening character when the salivary secretions return to normal.

Plummer-Vinson Disease. The lesions of this syndrome (esophagitis, dysphagia, spasm of the pharyngo-esophageal sphincter, anemia, glossitis) were originally believed to be present only in the esophagus, but more recent investigation has revealed that they usually effect the mouth and pharynx as well. It is found more often in women than in men, and especially in Sweden where Ahlbohm[1] has established the fact that it is definitely a precancerous lesion. Hypoproteinemia and avitaminosis B are associated as the main etiologic factors. Since the lesions almost always improve or disappear following the administration of a high protein diet supplemented by vitamin B, the disorder is undoubtedly a deficiency disease.

A typical example of this syndrome came under our observation several years ago in a woman of sixty years, with advanced esophagitis, sore mouth, malnutrition and neuropsychiatric disturbances. She habitually consumed between one and two quarts of gin daily and often went for periods of several days without taking any food whatever. At that time we did not suspect the deficiency nature of the disease and therefore she did not receive vitamin therapy. While in the hospital under observation for the cause of her esophagitis she improved markedly on the regular hospital diet with a reduction of the alcohol consumption. After leaving the hospital she resumed her former habits and died within a few months, ostensibly of chronic alcoholism. It is now plain to us that the basic cause of death in this case was complications of a severe vitamin deficiency.

Lesions of the Mucosa of the General Gastrointestinal Tract. While the most pronounced local subjective and objective mucous membrane symptoms occur in the mouth, these abnormal changes undoubtedly involve other portions of the gastrointestinal tract. The abundant sensory nerves of the oral cavity and the ease with which the mouth can be examined probably give an exaggerated picture of localization of these lesions in this area. Nevertheless, the appearance of the tongue has long been considered an index to the health of the rest of the alimentary canal. As Lewis[19] has remarked, "Raw red tongue, raw red gut."

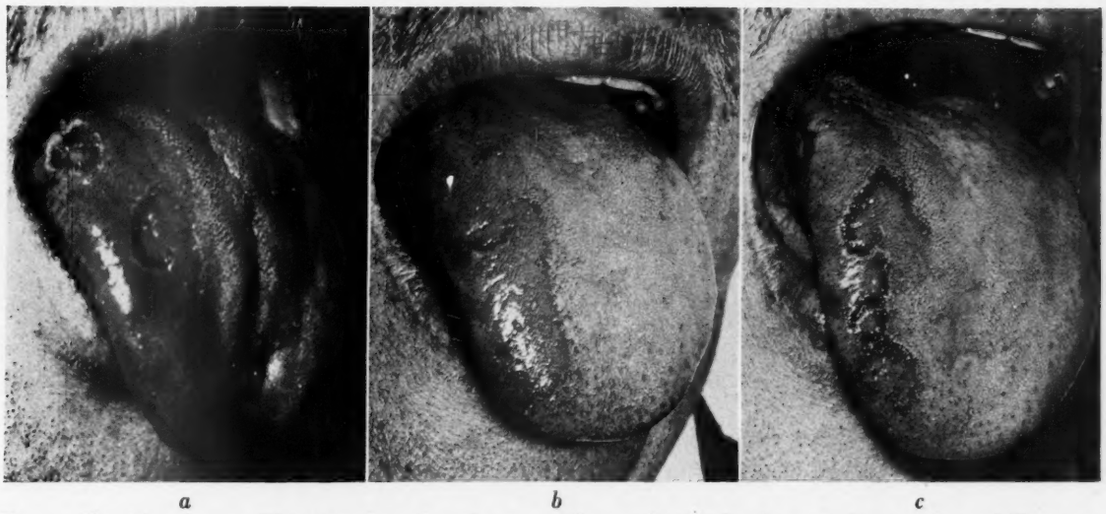
In cases of stomatitis of avitaminosis B, such symptoms as anorexia, indigestion, malnutrition, and constipation, suggest the presence of mucous membrane abnormalities in the stomach and intestines. Mackie, Miller and Rhoads[21] and Plummer[31] have demonstrated roentgenographically altered motor activity in the small intestines as a result of a vitamin B deficiency and they have shown that these abnormalities improve after specific therapy. Mackie[20] notes that the changes which occur in the small intestine in deficiency states are similar to the conditions present in the intestine of the very young baby whose nervous system is immature. He believes that these deficiency patterns are caused by some impairment of the functioning of the nervous system of the small intestine, caused by avitaminosis. Golden[14] also attributes the intestinal dysfunction to damage to the intramural nervous system.

The evidence is plain for at least a tentative diagnosis of avitaminosis B when an inflammatory oral mucosal lesion is associated with one or more of the following symptoms: malnutrition, mental depression, nervousness, insomnia, constipation, dermatoses and onychodystrophy. It is an interesting field for speculation and further investigation as to whether the incidence of an associated stomatitis (indicative of a B deficiency) is not more frequent in persons suffering from esophageal, gastric and rectal cancer than in those not so afflicted. Such investigations are now in progress at Memorial Hospital.

DIFFERENTIAL DIAGNOSIS OF THE INTRA-ORAL LESIONS OF AVITAMINOSIS B

As we have previously mentioned, the various forms of acute and chronic degener-

ative changes in the oral mucous membranes produced by a deficiency in the vitamin B complex, are not peculiar to this condition alone, but in many respects are identical in appearance with those produced by other forms of chronic irritation. When a composite clinical picture has been produced by several forms of chronic irritation, the clinical history and laboratory tests (Wassermann, liver function, etc.) may be of assistance in determining the responsible agents, but the differential diagnosis must be based mainly upon the response to therapy (dietary, antileuetic, etc.) or the effect of the elimination of the various suspected offenders (smoking, dental trauma, etc.).



a *b* *c*

FIG. 7. *Glossitis migrans.* Photographs *a*, *b* and *c* were taken at intervals of two to four weeks and illustrate the changing character of the lesion. Vitamin therapy gave little benefit.

There are certain clinical syndromes which should lead the observer to suspect a dietary deficiency and which should suggest a therapeutic vitamin test, for example, the atrophic tongue with injection of the mucosa and scanty, sticky saliva.

Glossitis Migrans. Although similar in some respects to the lesions produced by avitaminosis B, glossitis migrans is a disorder of the tongue of unknown origin which is seldom improved by vitamin B therapy. It consists of a sharply demarcated, heavily furred curved border of varying length, and about 3 to .5 cm. in width. Within the curve of this border the normal furring of the tongue is absent. The furred border of the lesion progresses outward at the rate of several millimeters a day, parts of it tending to fade out at the edges. Other second or third linear lesions may arise and progress outward from the point of origin, so that sometimes there are as many as three visible arcs. In rare instances the curved linear border consists of intense inflammation with a fibrinous exudate rather than an increase in furring. If observed at intervals of two or three days, the appearance is never the same. (Fig. 7.) Some patients with this lesion feel better systemically under vitamin B therapy, but in our experience, this seldom has any effect on the local lesion.

FREQUENCY OF VITAMIN B DEFICIENCY IN PATIENTS WITH MOUTH CANCER

From the foregoing descriptions of symptoms and signs of avitaminosis B, it will be apparent that the clinical picture is not clear cut, and that it would be impossible to separate a group of individuals into two definite classes, one with conclusive evidences of vitamin B deficiency and the other with no evidence whatever. No laboratory test has been devised which furnishes an accurate basis for this determination. For this reason, there is as yet no method of determining the absolute inci-

dence of avitaminosis B in mouth cancer or precancer. The proof of such dietary inadequacy is found in the fact that a large percentage of patients with mouth cancer do manifest one or more of the general and local abnormalities, and that these are almost always improved by administration of vitamin B. In brief, although no statistical proof can be presented, it is undoubtedly true that most patients with mouth cancer are suffering from an inadequate intake of the B complex to some degree at the time of admission. As proved by the therapeutic test, the same is true of most patients with precancerous mouth lesions, and it is therefore probable that the mucous membrane changes of avitaminosis B are more common and of more importance than those of all the other chronic irritants combined.

AVITAMINOSIS B AS A PROBLEM IN THE TREATMENT OF INTRA-ORAL CANCER

If one accepts the postulates already outlined, that a majority of patients with intra-oral cancer have avitaminosis B on admission—a condition which existed prior to and was at least partially responsible for the development of the cancer—the relief of this deficiency is an important part of the treatment of mouth cancer. When the intra-oral growth extends and becomes infected, or when aggressive treatment is instituted, either surgically of radiologically, mastication and swallowing become painful, and the sense of taste and the appetite are lost so that there is little inducement for the patient to eat properly. The acidity of fruit and vegetable juices (one of the normal sources of vitamins) is irritating to the inflamed mucosa. The necessarily soft or liquid diet in these cases tends to grow progressively restricted, and if not medically, will in most cases finally consist mainly of milk and raw eggs.

As a result, practically all patients with intra-oral cancer eventually develop an avitaminosis, whether or not it existed in the beginning. As the local symptoms increase in severity, mental depression and nervousness are aggravated. The best proof of the underlying cause of this train of symptoms is the almost certain improvement if not complete relief which follows an adequate vitamin intake.

In the patient with cancer, the depressing psychological effects of the knowledge or suspicion that he has cancer, is often the cause of more suffering than any organic effect of the malignant tumor. It is in these situations that vitamin therapy makes one of its most valuable contributions. A great deal has been written about the psychic management of patients with cancer, especially as to whether they should be informed of the true nature of their disease. Whether the patient is told the truth or merely suspects it, he will nevertheless be better able to face his misfortune with fortitude if he is not handicapped by the pessimism and melancholia which accompany avitaminosis B. In any disease as wasting and depleting as mouth cancer, the maintenance of proper nutrition is essential to successful treatment of the favorable cases as well as in palliation of the incurable.

DIETARY CAUSES OF AVITAMINOSIS B, OF PRECANCEROUS ORAL LESIONS AND OF MOUTH CANCER

We have maintained that the intra-oral lesions of avitaminosis B were precancerous and that some degree of avitaminosis was present on admission or developed during the course of treatment in practically all cases of intra-oral cancer. While these theories seemed perfectly sound to us from the empiric standpoint, we considered it only proper to test their validity by an investigation of the dietary habits of patients with intra-oral cancer and of patients with precancerous lesions of the oral mucous membranes, using as controls healthy persons with no intra-oral complaint. It was assumed that such a study would reveal whether an insufficient intake of the vitamin B complex, as shown by the dietary habits, was mainly responsible for the vitamin deficiency or whether such a

deficiency was due to an abnormally high individual requirement. This survey occupied a period of several months during which one of us (C. E. K.) interviewed some hundreds of patients with regard to their dietary habits, making a careful record of the presence or absence of intraoral abnormalities.

Three groups were studied, care being taken to assure uniformity with regard to the average age and sex distribution. Series I consisted of 100 patients from the clinic with definite precancerous oral lesions of the oral mucous membranes, all of whom presented one or more of the objective findings already outlined in a previous section of this report. Since leukoplakia alone is present in such a large percentage of the population, no patient was included in Series I who did not present some specific precancerous lesion other than leukoplakia.

Series II consisted of 100 patients with cancer of the mouth chosen at random from the Head and Neck Clinic at Memorial Hospital.

Series III (controls) consisted of 100 patients from the clinic (mainly those with facial skin cancer or relatives of patients) who appeared to be in excellent health and whose oral mucous membranes were essentially normal.

RESULTS OF INVESTIGATION OF DIETARY CAUSES OF AVITAMINOSIS B

Method of Survey. The estimation of the vitamin content of a diet from history alone is subject to considerable error since the calculation must be made on hearsay evidence alone. The following safeguards were used in the present investigation: (1) Unhurried interviews, avoiding leading questions; (2) the use of low minimum standards of vitamin requirements; (3) separation of those with adequate diets from those with inadequate diets by interposing a suboptimal group. The latter cases were considered indeterminate and were not included in the final calculations; (4) an allowance for loss of vitamins by cooking; (5) estimation of food juices consumed, and (6) calculation of diets on a weekly basis.

Various types of foods were classified loosely according to their vitamin B content, for example, leafy green vegetables, roots, legumes, fruits, seeds, cereals, meat and milk products, respectively. During the interview a typical week's menu was obtained from each patient, and each was then asked specific questions about the various food groups contained in his diet in order to have a double check on his dietary history. Peculiarities and fads of diet were recorded.

The daily intake of thiamin was used as an indication of the vitamin content of the diet. This fraction rather than any other was selected because of its widespread use as a survey factor and because its average daily requirement has been more definitely established than those of the other B components. Although a calculation of B_1 in the diet is not a highly accurate measurement of the other B fractions present, nevertheless, for our purposes it is a valuable indication of the general content of the vitamin B complex, with the possible exception of nicotinic acid.

The thiamin content of the individual diets was calculated in International Units according to the food values of Bowes and Church,[3] and two final calculations were made: First, the averages of the B intake in each of the three series were compared. Secondly, the percentage of adequate and deficient diets in each of the three series was calculated. In the latter calculation, the suboptimal group was omitted since we believe that this group contains a large number of borderline cases which had best be considered indeterminate.

Standards. The standard vitamin requirements of Munsell[28,29] were used, because of their wide acceptance and the fact that she employs as low a minimum requirement as any in common use. This low minimum serves to insure that diets considered low in the present survey are actually below the normal. In this manner, 2,100 International Units of B_1 per week

was considered adequate. Since any exact minimal figure must be considered arbitrary, a suboptimal group was included, made up of diets between 2,100 and 1,400 units per week. Diets containing less than 1,400 units per week were classed as deficient.

On a weekly basis, then, the figures are as follows:

Adequate..... 2,100 or more International Units B_1 (7 mg.)
Suboptimal..... 1,400 to 2,100 International Units B_1 (4 to 7 mg.)
Deficient..... Less than 1,400 International Units B_1 (Less than 4 mg.)

Results of Dietary Survey. As might be expected, the calculations of the vitamin content of these diets reveals considerable irregularity. The significant trend is seen in the averages of the whole groups and (excluding the suboptimal cases) in the relative numbers of adequate and deficient diets in each of the series. These averages are given in Table II.

In evaluating the clinical significance of these figures we have applied the statistical method as outlined by Campbell[4] and found our figures to be statistically reliable; that is, the differences between the sets of percentages compared may be considered due to factors other than chance. Any figures derived from the suboptimal group had best be considered inconclusive, since the classification of a given diet as suboptimal may depend upon errors in the interpretation of the dietary histories or upon moderate variations in the individual's vitamin requirement. That the economic status of the patient is of some importance from the standpoint of adequate diet, was shown by the fact that in the stomatitis group there was a higher percentage of deficient diets among clinic patients than among private patients.

The similarity of distribution of adequate, suboptimal and deficient diets in the stomatitis and mouth cancer series seems to us to be strong indication that they have the same dietary habits, and that individuals with deficient vitamin B diets have a greater tendency to develop intra-oral cancer than those on adequate diets.

In an investigation of this kind many paradoxical cases will be found, and it is

TABLE II

DIETARY SURVEY IN INTRA-ORAL CANCER AND PRECANCER*

Group	B_1 Intake				
	Weekly Average	Percentage of a Given Series			
		Adequate B_1 Per Cent	Inadequate B_1 Per Cent	Suboptimal B_1 Per Cent	Deficient B_1 Per Cent
Series I (100 cases) Stomatitis	1690 I.U. (5.6 mg.)	30	70	47	23
Series II (100 cases) Intra-oral cancer	1865 I.U. (6.2 mg.)	34	66	47	19
Series III (100 cases) Normal controls	2215 I.U. (7.4 mg.)	49	51	46	5

* The average weekly intake of vitamin B_1 in the stomatitis series (1,690 I.U.) and in the mouth cancer series (1,865 I.U.) is about 25 per cent less than that in the normal controls (2,215 I.U.).

Although about half of the controls consumed inadequate diets, only 5 per cent were definitely deficient. In the stomatitis and mouth cancer series 70 per cent of the diets were inadequate with over 20 per cent definitely deficient. In brief, definitely deficient diets appear to be about four times as frequent in the mouth cancer and stomatitis groups as in the normal controls.

plain that the existence of an avitaminosis cannot always be demonstrated by a survey of the dietary histories alone. In our Series III (normal controls) there were a number whose diets were definitely deficient, that is, containing less than 1,400 International Units of B_1 per week. Furthermore, in Series I among those patients who had advanced lesions of stomatitis, there were some patients who according to their dietary histories, were taking adequate diets, that is, 2,100 International Units per week or more. The true nature of the stomatitis in the latter type of case was demonstrated by the improvement and even complete disappearance of the symptoms when the intake of B was raised to several times the normal requirement. Such an instance is illustrated in the following case report:

Case IV. J. F., a male cook, aged sixty-three, was first seen in October, 1937, with squamous carcinoma of the tongue. The growth was treated by radiation, regressed promptly, and has not recurred. When first seen there was an associated bald, deeply injected tongue, and as a part of his general treatment he was placed on routine doses of vitamin concentrates in the form of liver and yeast. Within two months after the beginning of treatment, he had gained twenty-five pounds in weight. The tongue remained completely bald after the radiation reaction had subsided. (Fig. 8.) The degree of injection varied inversely with the regularity with which the patient followed directions as to vitamin therapy.

About a year and a half after admission, his health seemed to decline, even though he had been consuming about three tablespoonfuls of yeast daily, together with large quantities of leafy green vegetables. From this point onward, his condition became worse and no form of vitamin B therapy seemed beneficial until he increased his intake of yeast to eight tablespoonfuls daily, a dose which few patients can tolerate without marked nausea and diarrhea. There was a consequent immediate improvement in the state of his oral mucous membranes and general health. Since that time he has continued on that dosage and we have found that if he temporarily discontinues or reduces the amount of yeast, his appetite becomes poor, he loses weight and the tongue symptoms are aggravated.

Fig. 8. Completely bald tongue in a patient (Case IV) who had squamous carcinoma of the tongue, and other degenerative changes in the oral mucous membranes when first seen in October, 1937. The growth regressed after radiation and has not recurred.

When first examined, he had acute symptoms of vitamin deficiency, that is, deep injection of the tongue and perleche. He gained twenty-five pounds while on vitamin therapy. His health began to decline during the past year and it was found that unless he takes eight tablespoonfuls of yeast daily, the symptoms become markedly intensified. Despite these high doses, his tongue remains completely bald with deep fissures at the angles of the mouth (perleche).

These cases in which massive doses of vitamin B must be taken in order to maintain health can be explained on the basis of marked individual variations in ability either to absorb or utilize ingested vitamins. Among those patients in the stomatitis and mouth cancer series whose diets we calculated as suboptimal (though not definitely deficient) there was actually a considerable number who presented unmistakable signs of avitaminosis, the explanation being that although their intake was not far below normal, their requirements were inordinately high.

Some investigators have suggested that nonabsorption of vitamins from the gastrointestinal tract may be caused by such disorders as enteritis, colitis, diarrhea, etc. Once vitamins are absorbed, it is thought that they are changed in chemical composition and their end products finally utilized in the liver. Disorders in liver function would, therefore, prevent the normal metabolism of these substances. Cowgill,[7] Bridges[3a] and others believe that the vitamin B_1 requirement varies in the individual with the rate of caloric exchange and increases with the body weight in febrile conditions, in hyperthyroidism and in pregnancy. Not all of these theories have been clearly substantiated experimentally.

Dietary Peculiarities. A review of the histories of patients in the stomatitis series reveals a curious collection of dietary abnormalities from a wide variety of causes. In some cases avitaminosis was brought on by medically prescribed but unknowingly deficient diets for such diverse conditions as peptic ulcer, gallbladder disease, obesity, colitis, etc. Some of these patients, convinced that an improper diet was the original cause of some particular disorder, had blindly followed an even more incorrect and vitamin deficient diet for a period of years, bringing on symptoms far more serious than the original ailment. In some instances the responsible physician had dropped out of the case; in others, he had continued to care for the patient and was himself unaware of the harm his treatment was doing.

Fad diets were common even among well educated and intelligent patients seen in private practice. Some of the fadistic tendencies were based on ideas original with the patient, others had come from radio talks and health columns in newspapers and magazines. In many cases there was evidence of a vicious cycle; that is, a dietary deficiency brought on a loss of appetite and lack of interest in food so that the patient progressively restricted his diet to those substances most easily and cheaply obtained, mainly pure carbohydrates. In Table III are listed some of the peculiar diets in this group. We might mention in this discussion that dietary whims do not always lead to deficiencies, since among the normal controls we encountered a number of fad diets which were obviously adequate in vitamins and which included such habits as drinking the water in which potatoes were cooked, using only whole wheat flour for baking purposes, etc.

TABLE III
INSTANCES OF ABNORMAL DIETS IN CASES OF AVITAMINOSIS

1. A wealthy eccentric usually ate only breakfast, and after that beer and onions when he was hungry.
2. A woman voluntarily accompanied her husband on a diet for his peptic ulcer.
3. A woman prescribed for herself a diet for gallstones.
4. A woman restricted herself to a 1,000 calorie diet.
5. A mortician ate no vegetables and had a phobia for certain meats and fowl.
6. A traveling salesman ate a diet deficient in quantity and usually consisting only of sandwiches because he feared dirty food.
7. A woman ate no food juices, fruits, nor eggs and was on a liquid diet for three weeks prior to the onset of the stomatitis.
8. A dentist followed a combination of successively prescribed diets to the extent that he ate only lamb chops, soda crackers, applesauce, plain cake and cream.
9. A man ate neither meat nor vegetables.
10. A female peddler ate bread, butter, eggs and fruit exclusively.
11. A paretic beer salesman drank beer when hungry.
12. A woman avoided pork, fruit, eggs and milk because two members of her family were on diets eliminating these foods. In addition, she limited herself to 1,000 calories a day in order to reduce.
13. Two patients followed medically prescribed reducing diets.
14. A nurse followed a self-prescribed diet for gastroptosis and peptic ulcer, the latter of which she did not have.
15. Three patients were on grossly inadequate diets because of their financial status.

It is probable that the most frequent underlying cause of an inadequate vitamin intake lies in individual personality factors such as peculiar dietary prejudices formed in childhood and often based on racial, nationalistic or provincial family customs. Idiosyncrasies are commonly met with in temperamental, impressionistic individuals, some of whom refer to all vegetables as "rabbit food." Such temperamental whims may be either the cause or the result of a

vitamin deficiency. When they are both, a vicious cycle is set up. In women, deficient diets are often due to the fear of gaining weight. In most city dwellers there is the tendency to eat at "quick lunches" and drugstore counters, where green vegetables and fresh meats are replaced by carbohydrates in the form of sandwiches, ice cream, malted milk and pastry.

Chronic Alcoholism. Since alcohol can be oxidized in the body to produce energy, and thereby replace carbohydrates and to some extent, fats, chronic alcoholics can live for considerable periods provided that they ingest minimal quantities of proteins to replace protein and mineral waste. The degree of chronic alcoholism is variable, since some patients replace only a part of their diets with alcohol. In any case, the energy-producing alcohol is almost a pure chemical and contains neither vitamins, proteins nor minerals.

It has long been believed by those engaged in vitamin research that the neuritis, some of the psychoses and other general effects of chronic alcoholism were mainly due to a vitamin B deficiency. The validity of these theories had been supported by the work of Minot, Strauss and Cobb,[27] who found that the neuritic symptoms of alcoholism could often be relieved by the administration of the vitamin B complex without any decrease in the consumption of alcohol or other increase in the vitamin content of the diet.

It has been our observation that the deficiency symptoms in chronic alcoholism sometimes consist chiefly of malnutrition and degenerative precancerous changes in the oral mucous membranes. It is our opinion that the significance of alcohol in the etiology of mouth cancer lies in its capacity to produce the stomatitis of vitamin deficiency rather than to its local irritative effect on the oral mucosa. The following case report illustrates our view:

Case V. P. P., a male, aged sixty, first came under our observation because of epidermoid carcinoma of the posterolateral border of the tongue. At the time of the first examination, it was noted that the mucosa of the entire tongue was deeply injected with partial atrophy of the papillae along the edges and hypertrophy over the dorsum. The growth was treated by radiation and completely regressed, the patient remaining free of cancer for about eighteen months. He then developed a second primary lesion in the anterior floor of the mouth. This second primary was also treated successfully by radiation. The patient then remained free of local cancer until the time of his death two years later from pulmonary metastases.

During the three-year period between the first development of his tongue cancer and his death, he was under close observation and it was noted that the acute or subacute glossitis never completely disappeared. The inflammatory symptoms improved whenever the patient could be persuaded to take a reasonably adequate diet, supplemented by vitamin concentrates, but the glossitis always immediately became aggravated when his dietary habits returned to their customary irregular character. At such times the tongue would become acutely inflamed and tender and the saliva scanty and sticky. These relapses were accompanied by an increase in his psychoneurotic symptoms and a marked loss of weight.

In his youth he had inherited a large fortune which insured him of an adequate income and left him free to indulge the whims and erratic tastes of a constitutionally unstable personality. He was tempermental, strongly opinionated and prejudiced in his dietary habits and had an intense dislike for certain foods, especially green vegetables and meat. He was convinced that the most wholesome and entirely satisfactory meal for him was a raw egg with a glass of sherry twice a day. He had formerly consumed moderate amounts of whiskey, which his family physician had finally induced him to give up; but he continued to take generous quantities of ale and champagne, which, despite medical advice, he firmly believed to contain only a small percentage of alcohol.

Although he was five feet, eight inches tall, he stated that he had never weighed more than 120 pounds. While under treatment for his tongue cancer his weight varied between a high of 130 pounds on a carefully regulated diet, and a low of 110 pounds when he resumed his usual dietary habits. During the last three

years of his life, despite persistent medical attempts to correct his diet and vitamin intake, he became progressively more difficult to control and often rebelled for periods of several weeks, during which times he subsisted on minimal quantities of milk, raw eggs with sherry, ale and champagne. The stomatitis persisted, always becoming more severe at the times of reduced vitamin intake. There were progressive degenerative changes in the oral mucous membranes and it is probable that had he survived he would have developed a third or even more primary cancers of the mouth.

The association of causes and effects in this case seems rather obvious to us, that is, the inherent personality weaknesses leading to an unhygienic mode of life, sufficient wealth to obviate the necessity for any discipline or restraint in indulging the various whims and irregular habits including chronic alcoholism, avitaminosis, precancerous stomatitis and finally multiple mouth cancers.

TREATMENT OF AVITAMINOSIS B

There is apparently little storage of excess vitamin B in the body beyond the current need, and deficiency symptoms occur within a few days after withdrawal of the vitamin source. For this reason, any effective treatment must be made part of a frequently repeated and regular routine. Furthermore, the quantities of the various fractions of the B complex necessary to prevent deficiency symptoms are specific for each individual. When a marked avitaminosis has developed, a partial remedial dose will have little effect on the condition, and relief will not be obtained until the full necessary amount is administered.

As we have already mentioned, there is a wide variance between the minimum requirements in health (which have been established experimentally) and the therapeutic doses necessary to obtain the maximum benefit in cases of spontaneous vitamin deficiency. For example, although 1 mg. of thiamin and 2 mg. of riboflavin have been found to be required for the maintenance of health in the normal adult, these quantities when administered to a person suffering from severe avitaminosis, will rarely produce the maximum beneficial effect, and in most cases will not cause any noticeable improvement.

We have found it advisable, when using natural concentrates such as yeast and liver, to provide from five to ten times the normal minimum requirement of thiamin and riboflavin, or 30 to 45 Gm. (2 to 3 tablespoonfuls) daily of granular yeast. In exceptional cases the maximum relief cannot be obtained unless inordinately high therapeutic doses are consumed, as for instance, one of our patients who ingests about 240 Gm. (two teacups) of brewer's yeast a day and who insists that unless this amount is taken, marked asthenia and mental depression occur.

Large doses of thiamin, riboflavin and nicotinic acid produce certain toxic effects which vary among individuals. Although 50 mg. of nicotinic acid is considered by some investigators to be a minimum daily requirement in health, this amount, if taken in a single dose, will produce in most persons the temporary symptoms of burning sensations and visible flushing of the skin. It is curious and possibly of some significance that these manifestations of overdosage resemble in some respects the chronic skin lesions of nicotinic acid deficiency (pellagra). Abels, of Memorial Hospital, in an unpublished experiment has found that daily doses of 100 mg. of thiamin (100 times the normal requirement) produce nervousness, irritability and insomnia. In this case also, the symptoms of overdosage and underdosage appear to be similar.

At one time during the progress of these clinical investigations we administered riboflavin in excessive doses (20 mg. daily) to several patients. While this quantity produced little improvement in the mucous membrane lesions of the avitaminosis, all patients suffered from such toxic effects as dimness of vision, burning of the eyelids and conjunctivae, frontal headache and some anorexia. On the other hand, moder-

ate overdosage (about five to ten times the minimal requirement in health) rarely produces any toxic effects, and from the practical standpoint is advisable when natural concentrates are used to supplement the diet.

At the present time it is difficult to explain adequately the necessity for, and the beneficial action of such high doses (five to ten times normal) of the known components of the B complex when taken in the form of the natural concentrates, namely, liver and yeast. One reasonable explanation might be the existence of essential but unidentified fractions occurring in comparatively small quantities in the natural concentrates. In any case, the requirements of individual patients either for the synthetic commercial combinations or for the natural concentrates can be determined only by therapeutic test.

The basic treatment for avitaminosis B, as for any deficiency disease, should be to supply as much as possible of the inadequate element in the form of natural foods. The patient should be directed to take at least twice daily, generous servings of green vegetables (peas, string beans, lettuce, asparagus, broccoli, etc.) properly cooked, that is, preferably steamed in a pressure cooker for a short time with a minimum of water, and conserving the juices. For patients who require a soft or liquid diet, sometimes taken through nasal feeding tubes, the vegetables after the same careful cooking can be pureed.

It is doubtful whether the quantities of glandular meats such as liver and kidney can ever be increased in the diet of the average person, so as to make any significant difference in the vitamin intake because these foods tend to become distasteful if eaten too often. For this reason it is more practical to stress the ingestion of several high vitamin B foods such as the legumes, pork, and the whole wheats rather than a single excellent source of the vitamin which is likely to prove loathsome to the patient after a short time.

The modification of an inadequate diet cannot always be depended upon completely to relieve the symptoms of a severe deficiency, and it is usually necessary or at least expeditious to supplement the diet with natural concentrates and occasionally with specially prepared combinations of the more important B fractions. A number of such preparations have been put up in the form of tablets or solutions for both oral and parenteral administration. In cases of marked deficiency, the doses should be purposely high even to the point of tolerance.

In some instances the administration of a single fraction of the vitamin B complex (thiamin, riboflavin, nicotinic acid, etc.) may cause marked improvement, but combinations of the known fractions almost always give better results. In general, the maximum benefit is obtained through use of such natural concentrates as yeast and liver. This fact, noted also by Elsom[10] and others, may be explained by assuming the existence of certain essential components of the B complex not yet isolated and identified, and for that reason, impossible of inclusion in any present day synthetic preparation. The superiority of a combination of several fractions rather than a single one might also be due to an essential synergistic action of the components.*

Although the symptoms of avitaminosis may often be relieved completely by proper diet and vitamin therapy, life-long supervision of the patient's diet, sometimes with vitamin concentrate supplements, will be required. The necessity for the prolonged use of vitamin concentrates makes the expensive synthetic commercial preparations unsatisfactory for the average patient,

* It is also undoubtedly of significance that a daily dose of 45 Gm of yeast provides about 40 Gm of available protein. According to Best,[2] these proteins contain such sulfur-amino-acids as methionine, cysteine and choline. These three substances increase the capacity of the organism to utilize proteins and fats. If there is an associated fatty infiltration of the liver due to a B deficient diet, the sulfur-amino-acids and choline, if ingested in sufficient quantities, will act as lipotropic agents. When the liver has been depleted of excess fats by their action, the efficiency of this organ is increased.

who will tend to discontinue treatment and suffer relapse rather than endure the financial burden imposed upon him by such therapy. We, as well as others, have found liver extract powders and solutions about as effective as yeast in the treatment of vitamin B deficiency. As Elvehjem[11] has stated, it is probable that liver contains all the factors of the B complex. The objection to liver is that it is both unpalatable and fairly expensive. Powdered liver extract in doses of 12 Gm. (three teaspoonfuls) daily will cost between three and four dollars a week.

Brewer's yeast is probably the most satisfactory and best all-round natural B concentrate. This substance is available in a number of forms such as dried granular solid, pastes, compressed cakes and tablets. All of these crude forms are satisfactory with the possible exception of the compressed tablets which almost always mislead patients and even physicians into an unwarranted confidence in their strength and therefore to underdosage. The potency of liquid extracts of yeast is uncertain, since the residue discarded in their preparation probably contains essential vitamin fractions.

In our experience one of the most satisfactory yeast preparations, from the standpoints of potency, cost and palatability, is granular dried yeast. When taken in doses of 30 to 45 Gm. (two to three tablespoonfuls) daily, the cost is not more than one dollar a week. Paste forms of yeast are usually several times more expensive and less palatable to the average person. Both the taste and the odor of dried granular yeast are repugnant to some patients, and in a few, therapeutic doses cause indigestion flatulence, diarrhea and even nausea. For these individuals it is best to try some other form of yeast or to substitute powdered liver extract or one of the commercial synthetic combinations for mouth or parenteral administration. If 45 Gm. (three tablespoonfuls) causes any distress, the dose should be reduced by one-third or one-half. It is of significance that many persons do not distinguish between tablespoons and dessert spoons and also that there is considerable disagreement as to what constitutes a heaping spoonful. As a result of such discrepancies, the quantity can only be approximately estimated.

The least disagreeable method of taking the granular yeast is to place it dry in the mouth and then wash it down with a beverage. It may also be taken with a mouthful of chewed food and washed down. Some patients prefer to spread it on cereal or bread or to mix it with orange or tomato juice. For those patients on a liquid diet or for those fed through nasal tubes the granular yeast, yeast paste or powdered liver extract should be dissolved in warm water and then added to the feeding.

Some patients prefer the ordinary compressed yeast cakes sold in grocery stores for household purposes (baking, etc.). Six cakes a day corresponds approximately to three tablespoonfuls of the dried granular brewer's yeast, and while equally effective, the yeast cakes will be somewhat more expensive than the dried granular form.

The Response of Precancerous Stomatitis to Vitamin B Therapy. The clinical course of the mouth lesions of avitaminosis B under specific therapy is not uniform. In some instances the local and general symptoms are entirely relieved and the mucous membrane of the mouth returns to normal. In others there may be a marked improvement in the local and general symptoms with permanent disappearance of acute inflammation, healing of ulcers, relief of pain, etc., but with the persistence of papillary atrophy or hypertrophy and leukoplakia. In a few instances after an initial improvement in both local and general symptoms on vitamin therapy, even though the remedial dosage is continued or increased, there may begin after a period of one or two years, a recurrence of the signs of avitaminosis. In some cases these symptoms cannot be relieved by vitamin therapy, although unusual increases in dosage may tend to slow down the progress of the disorder.

Under vitamin B therapy, the acute mucous membrane lesions of avitaminosis B (inflammation, ulceration, pain, tenderness) will usually disappear or at least improve. During treatment for cancer the subjective symptoms of acute local radiation reactions are also less distressing if provision is made for adequate B intake. In patients with mouth cancer, such associated symptoms as anorexia, indigestion, constipation, nervousness, mental depression and insomnia all tend to subside or even to be eliminated completely when such precautions are taken. If the patient is markedly undernourished, there will almost always be a gain in weight. In the present series the average increase among those who gained any weight at all was twenty-five pounds, the greatest gain in any individual being thirty-nine pounds. The benefit to the patient with cancer undergoing aggressive treatment, of such an improvement in the general health, needs no further emphasis.

In precancerous stomatitis of avitaminosis B, the degree to which the degenerative changes in the mouth, particularly in the tongue, will return to normal depends upon the extent and duration of such changes.

a *b*

FIG. 9. M. F., female, now aged sixty-three, has been observed at Memorial Hospital for twenty years because of "sore tongue." In 1921, the tongue was described as "geographic." In 1939, the patient returned after an absence of over a year because of an increase of the soreness of the tongue and fissures at the angles of the mouth. *a*, At that time it was discovered that she had been living on a diet of white bread, butter and tea for over ten years. She was also suffering from pernicious anemia. The patient was somewhat irregular in her visits and unco-operative with treatment for over a year during which there was some improvement in the tongue. She was finally induced to take yeast and intramuscular liver extract regularly, following which treatment the perleche healed and the scrotal appearance of the tongue practically disappeared, with partial regrowth of the papillae *b*, and with marked improvement in the blood count, which returned to normal.

(Fig. 9.) We have mentioned that the papillae will not regenerate when atrophy has progressed to the point where the mucosa of the dorsum of the tongue resembles that of the cheek. When the atrophy is moderate or when the deficiency is acute and of short duration, there is often a prompt return to the normal state. In brief, when the stomatitis of avitaminosis B has been present for a long time, the degenerative changes in the oral mucous membranes are not reversible but will remain permanently, even though the dietary deficiency has been corrected.

VITAMIN B AS A SUPPLEMENT IN THE TREATMENT OF INTRA-ORAL CANCER

Supplementary vitamin B therapy should be a part of the routine during the treatment of all patients with mouth cancer. It should be the purpose to effect at least a slight gain in weight during the first one or two months of treatment, especially during

radiation therapy. Such a weight gain (marked in those who are admitted with severe malnutrition, and moderate in those who appear to be of average nutrition) is one of the most important means of building up a reserve of resistance to the debilitating effects of the necessarily aggressive treatment, either radiologic or surgical.

The diet of these patients must be closely supervised and directed. In chronic alcoholics the alcohol consumption should be radically decreased if not eliminated entirely. The caloric intake should be 3,000 to 3,500 calories a day if possible. Stress should be placed on the use of leafy green vegetables and other foods which have a high vitamin content. If the diet must be soft or liquid, as in tube feedings, these vegetables must be pureed.

Finally and of equal importance, supplementary natural concentrates of vitamin B should be prescribed. As we have already noted, from the standpoint of efficiency and cost, the most practical are the crude preparations of yeast. If these preparations cannot be tolerated, the more expensive yeast pastes or liver extract powders may be used perorally, and if these, too, are objectionable, one of the synthetic concentrates (combinations of thiamin, riboflavin, etc.) should be employed. If the peroral route cannot be used, the liver concentrates or the synthetic preparations should be given parenterally. No patient with intra-oral cancer should be subjected to radiation or to a major surgical procedure without the benefit of vitamin therapy.

SIGNIFICANCE OF PROPER DIET IN THE PROPHYLAXIS OF CANCER

Since it is impossible to demonstrate conclusively the existence of vitamin B deficiencies except by therapeutic tests, one can only say that such deficiencies play an important part in the production of irritative, and hence precancerous lesions of the mouth. Nevertheless, the clinician who, in the treatment of intra-oral cancer and precancer, takes the trouble to prescribe routinely vitamin B therapy, and who observes the clinical response, can have little doubt as to the significance of avitaminosis B in the etiology of malignant tumors of the mouth. If the clinician will also note the condition of the oral mucous membranes in apparently healthy normal persons, he will be impressed by the prevalence among the entire population of the local and general symptoms of mild to severe vitamin B deficiencies.

If one accepts the postulate that the degenerative changes in the oral mucous membranes which result from avitaminosis B are important precancerous lesions, it is reasonable to believe that similar lesions from the same cause are frequently associated and of significance in cancer of the entire gastrointestinal tract (which comprises more than half of all human cancer). These theories, if sound, may have wide practical importance in the prophylaxis of gastrointestinal cancer, but there are certain obstacles in the way of their general acceptance by the medical profession, public health authorities and the lay public. It would be easier to impress both physicians and the laity if it could be maintained that there is one sole cause for cancer and precancer, and that there is one simple remedy which, taken in pill form, so many times a day for a few weeks, would effect a lasting cure and a preventative of the basic abnormality. In order to relieve avitaminosis B, however, the mode of life must be permanently modified, that is, the intake of vitamins must be increased and maintained as long as the patient lives. Such a permanent régime will, in many cases, become tedious since it is not supported by the emotional stimulus which accompanies a shorter, more intense course of therapy.

The recent widespread publicity concerning vitamins has undoubtedly been beneficial in that it has made both the profession and the laity vitamin conscious. It is difficult, however, for the average layman to interpret correctly the significance of such scientific information even though it

may be presented to him purposely in the simplest terms. At the present time vitamins are of considerable public interest which unfortunately is probably transient. In order appreciably to affect the general health by an increased vitamin intake, the hygienic dietary measures must be made the responsibility of the individual, for it is obvious that no significant number of individual diets can come under the personal direction and supervision of a physician. Furthermore, the remedy, in order to be popular, must be pleasant, inexpensive, and convenient; and the average layman, if left to his own resources, is likely to be misled into a dependence on the most expeditious though inadequate measures. As for instance, in the advertising of certain foods it is implied that deficiencies can be readily overcome by reinforcing the vitamin content of bread and cereals. In reality, since these foods do not make up a major portion of the average diet, there can be little benefit from such vitamin supplements unless inordinate quantities are consumed.

In the last few years the number of synthetic vitamin preparations which have been placed on the market has been so great as to cause considerable confusion. It is difficult and even impossible for the average physician to evaluate the merits of all of these different concentrates, most of which, although convenient, are expensive and lack some of the essential fractions of the B complex. Some drug firms have put up dried yeast in tablets containing about .6 Gm. (10 gr.) each; and whether or not specific directions are given, the average patient will assume that two or three a day (a common dose for many kinds of pills) are adequate, when as a matter of fact, it would require about seventy such tablets to supply the equivalent of 45 Gm. (three tablespoonfuls) of dried granular brewer's yeast.

It is doubtful whether the problem of avitaminosis in the general public can ever be solved by the increased sale and consumption of vitamin concentrates in any form. Such substances find their main practical value in the treatment, under medical supervision, of aggravated cases of deficiency diseases. It is also unlikely that any large scale benefit can be derived from the reinforcement of a few food substances such as bread and cereals with such themostable fractions as riboflavin, or by the addition of any of the known fractions to milk.

The most satisfactory source of vitamins is in natural foods, and at least a partial solution of the problem would be to increase by propaganda and public health education the general consumption of green vegetables, fresh or canned, and fresh fruits and milk. Ruffin[33] lays particular stress on the importance of adequate diets rather than reliance on vitamin supplements. Efforts should also be made to improve methods of canning and cooking so as to preserve as much as possible of the natural vitamin content. Such a program would be helped if some means could be devised to decrease the use of sweets and desserts so that it would be necessary to obtain nourishment from other foods which are better sources of vitamins.

The only really effective method of attaining such an end would probably be by indirection, that is, propaganda designed to increase the consumption of vitamin-rich foods without laying any particular stress on the special benefits to be derived. It has been demonstrated in the past in the field of commercial advertising that such an increase or modification of dietary habits can be brought about by persistent advertising of certain foods and fruits.

It is of interest to note in passing that in the present day draft army there is an average gain in weight of several pounds, indicating that in general, the draftees had been on improper diets before their induction into the army. The most obvious explanation of this phenomenon is the assumption that the weight gain was due to an increased caloric intake. On the other hand, more careful consideration would suggest that the gain may have been

due in greater part to the fact that the army diet has corrected previous vitamin deficiencies.

The B complex is, of course, not the only essential vitamin group, but at this time and in this country it is probable that avitaminosis B is responsible for more ill-health than a deficiency in any other vitamin. If the prevalence of this deficiency could be reduced, it is reasonable to expect an improvement in the general health of the population, and a reduction in the incidence of gastrointestinal cancer and also certain forms of psychoneuroses, and in the final analysis, produce a salutary effect upon mass psychology and socio-political trends.

SUMMARY

The degenerative changes which occur in the oral mucous membranes as the result of avitaminosis B are discussed as to their etiology, symptomatology and treatment. The clinical material upon which this study is based is drawn from the general admissions to the Head and Neck Clinic of the Memorial Hospital and includes three special series in which dietary surveys were made. The significance of the mouth lesions of avitaminosis B is discussed from the standpoints of prophylaxis and treatment of mouth cancer.

CONCLUSIONS

1. Degenerative mucous membrane changes are found in the majority of cases of mouth cancer. These degenerative changes are usually the result of a combination of several forms of chronic irritation (tobacco, syphilis, sepsis, avitaminosis).

2. The most frequent and probably the most important form of chronic irritation, from the standpoint of cancerigenesis in the oral mucous membranes, is that of avitaminosis B.

3. Most patients with mouth cancer already are suffering from a mild to marked avitaminosis B on admission. This disorder tends to be aggravated by the necessarily restricted diet during the painful stages of mouth cancer. Supplementary vitamin therapy is one of the most important factors in the successful treatment of intra-oral cancer.

4. There is considerable clinical evidence that the mucous membrane lesions of avitaminosis B are not confined to the mouth cavity alone, but affect the whole gastrointestinal tract. It is therefore possible that such degenerative changes are of significance in the etiology of gastric and intestinal cancer as well as mouth cancer. It is reasonable to believe that one of the most effective means of prophylaxis against mouth cancer would be to increase the general intake of vitamin B in foods.

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MILITARY BURNS

AN ANALYSIS OF 308 CASES

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THE present day management of burns has been the result of many painstaking contributions in the last two decades. Until 1925, most burns were treated with expectancy and a patient with 40 per cent of body surface involved was given a generally hopeless prognosis. Most deaths had been ascribed to primary and secondary shock associated with the elaboration of some toxin at the burn site. In that year Davidson proposed his epoch-making tanning method which appealed more from simplicity in handling the patient. The general improvement in mortality figures from this type of therapy stimulated further investigation.

In 1930, Underhill showed startling relationships between the hematocrit concentration and mortality. In dogs who had as much as 20 per cent body surface burned, there was a universal rise of hemoglobin and red cells with a loss of as much as 70 per cent of body plasma into the tissues. The loss of plasma through increased capillary permeability was irreversible and had to be compensated by the intravenous administration of large amounts of fluids. Plasma chlorides were also rapidly depleted and Coller and Maddock advocated giving 0.5 mg. of sodium chloride per kilogram of body weight for each 100 mg. lost beneath the normal blood level of 560 mg. per cent. The recent advances in preparation of plasma and its use have been most effective in creating a normal protein balance and hematocrit percentage. Harkins developed a formula for administering plasma in that 100 cc. were given for each point of rise of the hematocrit over the normal of 45.

As early as 1933, Aldrich and Firor had challenged the toxemia theory. They claimed that, aside from initial shock, patients died from purely infection and sepsis. This evidence was based on numerous cultures taken from the burn site before and after application of the tanning agent, and revealed heavy cultures of hemolytic and nonhemolytic staphylococci and streptococci. They proposed careful débridement to the point of wound sterility before applying the tannic acid. Moreover, various dyes were proposed as gentian violet and later a triple dye composed of gentian violet, brilliant green and acriflavine to promote bactericidal action against any remaining organisms. Other investigators with the same mode of attack, proposed continuous wet dressing with azochloramid and applications of silver nitrate by either solution or stick. These methods were advocated alone or in combination with the tannic acid method, and frequently modifying both with the resumption of the time-worn ointment forms of therapy.

The availability of blood plasma for early treatment of shock, the careful débridement of the burn, and the development of the sulfonamides stand foremost in attaining our present-day results. The first consideration for any burned patient is for his life. Blood pressure readings are taken frequently, red cell and hemoglobin estimations are made, and the patient is given sufficient plasma to convert the hematocrit percentage to normal. Fluids and morphine are prescribed in adequate amounts until all evidence of shock is controlled. Most patients regardless of the degree or extent of the burn will respond to this treatment within three or four hours, and those who do not, will probably not respond to any form of therapy. In the

favorable group, the burn is then débrided thoroughly with aseptic technic. Green soap and water are used until the surgeon is satisfied that all foreign particles are removed. All necrotic tissue and vesicles are excised and the burn is lavaged with sterile water or saline. This débridement may require heavy doses of opiate to control pain, and it is believed that an adequate cleansing can be done with sterile gauze without resorting to the scrub brush. The latter instrument would appear to increase the amount of nonviable tissue and traumatize sufficiently to affect after-healing. Gentleness will in a good many cases of shock, mark the difference between a survival or death.

After thorough cleansing the burn is ready for one of the tanning agents. It is not believed that the end result is influenced by the agent chosen, and all forms have been used in this series with equal success. There is an apparent advantage in a 1 per cent aqueous solution of gentian violet, in that two or three applications usually suffice to provide a good crust. Ointments as boric unguentum, amertan, or gentian jelly are used on the face and fingers. Sterile mineral oil is dropped into the eyes and ears as long as there is swelling of surrounding tissues. The burned areas are then encased in sterile gauze for forty-eight hours until the crust gives sufficient protection alone. Motion of all joint surfaces is encouraged as soon as swelling has subsided, usually after forty-eight hours, and full range of motion is attained daily. This prevents contracture, promotes flexibility of the crust, and has not, in our hands, delayed wound healing.

In burns which are treated after twenty-four hours without proper débridement, or in those who present temperature elevation after seventy-two hours, a search is made for a focus of suppuration. If found, the overlying crust is removed and the part encased in continuous wet boric acid or saline dressings until all evidence of infection is absent. No attempt is made to reapply a tanning agent over previously septic areas as experience has shown that suppuration will recur. Ointments, on the other hand, are chosen and such dressings are changed daily, washing all ointment from the burn before applying it fresh. If no focus of infection is found, sulfathiazole is given orally in full therapeutic amounts to obtain a blood concentration of the drug of 5 or 6 mg. per cent. If suppuration exists, it will eventually become evident and may be then handled as previously advocated.

Table 1
CAUSES OF BURNS

	No.		No.
Gasoline	89	Lysol	13
Flame	47	Iodine	12
Hot water	41	Lye	12
Hot stove	19	Phosphorus	8
Hot ashes	11	$HgCl_2$	3
Hot metal	5	Cresol	3
Hot grease	5	Phenol	3
Hot water bag	3	Ammonia	2
Steam	3	H_2SO_4	1
Gunpowder	11	Gasoline	1
Hot tar	2	$KMnO_4$	1
Electric	1	SO_3	1
Sunburn	8	Co_2 snow	1
Ultraviolet	1	Gunpowder	1
Total thermal	246	Total chemical	62

If at the end of ten days the crust has not shown separation, wet dressings are applied to loosen it. In third degree burns, skin grafts are then applied to the granulation tissue base after complete removal of the crust. These have been either Davis pinch grafts or split-thickness grafts for joint surfaces. The usual pressure dressing is applied following the graft.

This analysis comprises a study of 308 patients admitted to the Station Hospital, Fort Benning, Georgia from January, 1927, to December, 1941. During this interval there were approximately 95,000 hospital admissions, burns representing a ratio of 1 to 300. All were male patients with the exception of one female child. The average age was 24.2 years with 93 per cent falling in the eighteen to thirty-five-age group. There were 266 white and forty-two colored patients, and twenty were considered mild enough to be treated as out-patients.

Table 1 shows the general causes of these military burns. Of the total, sixty-two were chemical and 246 thermal. Included in the latter are nine cases of actinic origin. Gasoline leads in order of occurrence as most of the vehicles and field apparatus are fueled with this commodity. The importance of this agent has increased steadily in the past few years. Actual flame contact is distinguished from gasoline burns inasmuch as the chemical factor of the fuel is not present. Most of the patients received flame burns in an attempt to extinguish a blaze, or from the explosion of some inflammable gas. This type of burn is distinguished again from contact with a hot object or hot material, as hot grease, tar and gunpowder, which may afford more prolonged and intense heat from their contact with the tissues. In the main, agents are important only as their chemical or thermal action is implied.

Table II
COMPLICATIONS

	No.		No.
Pneumonia	2	Corneal opacity	2
Cicatrix, painful	1	Shock,* severe	6
Symblepheron	1	Shock, moderate	23
Anuria*	1		
Nephritis, acute	1		

* Died.

The criteria for study of any burn management can be derived from the collection of the following data: mortality rate, complications and the length of stay in the hospital. The type and seriousness of burns in any series of cases will materially affect the mortality rate. Military burns on the whole are potentially serious but most of the patients are seen promptly by some medical attendant. Moreover, many burns of minor character are hospitalized which in civilian life would not be seen. These features have led to a strikingly low mortality rate of 1.3 per cent in the group. There were, in addition to the four deaths reported, four others who were dead before admission to the hospital. With the exception of one case, all patients involved in fatal cases died within twelve hours due to the extent of the burn, despite intensive shock treatment. The other patient died on the eighth day of total anuria secondary to sulfathiazole administration.

There were few complications as can be seen by Table II, and particular attention is called to the paucity of contractures. This, it is believed, can be attributed almost entirely to careful débridement and enforcement of early active and passive motion. Pneumonia, a fairly common complication in most lists, occurred but twice due to promptness in allaying any threat of the infection by the use of the sulfa drugs. Shock in varying degrees was present in most of the patients with 20 per cent or more of surface involved, but it was not credited for analysis unless it was present in the secondary or hemagenic form. Other complications which may develop were not present in this series. Septicemia is one of the most common complication and may lead to metastatic abscess formation elsewhere. Tetanus has been reported by Newberger in a number of patients, but most recent series do not show it. All of these patients received either a protective dose of antitetanic serum or a stimulating dose of tetanus toxoid on admission. Duodenal ulcer as described by Curling has been reported as fairly frequent by Pack and Davis. Occasional instances of carcinoma developing in

Table III
PERCENTAGE AREA OF BURNS

All Burns	Area, Per Cent	No.	Hospital Stay, Days
	1 or less	18	13.1
	2 to 5	155	18.0
	6 to 10	41	24.2
	11 to 15	15	20.2
	16 to 20	10	38.7
	21 to 30	4	37.2
	30 to 40	2	75.5
	Over 40	4	3.7—all died
Special burns			
Penis and genitalia	0.5	21	21.5
Actinic	33.3	9	6.3

the burn scar (Marjolin's ulcer) have been reported.

The length of stay runs parallel with the healing of the burn and it is an important measure for effectiveness of treatment. It is dependent upon (1) degree of the burn, (2) extent of the burn, (3) location of the burn, (4) type of agent, (5) concomittant injuries, (6) presence of infection and (7) treatment.

TABLE IV
DEGREE OF BURNS

	Degree	No.	Hospital Stay, Days
All burns			
308 cases	1st	114	11.8
c 374 burns	2nd	229	21.4
	3rd	31	49.9
Chemical			
62 cases	1st	28	
c 68 burns	2nd	32	16.1
	3rd	8	average

Most of these burns involved 5 per cent or less of body surface. Berkow's method of estimating surface area involved was utilized in Table III. There was little difference in hospital stay when the burn involved 5 or 15 per cent. Above this figure, hospital stay was remarkably prolonged. The average duration of treatment for all burns was 20.5 days. The degree of the burn varied directly with the time of healing and third degree burns required twice the time as second degree burns as can be seen from Table IV. The regions of the body burned were the hands, legs, forearms, head and neck, thighs, arms, chest, feet, genitalia, eyes, abdomen and buttocks in the order named. (Table v.) There is a distinct difference in healing time in burns of the genitalia as compared with other regions. While this region comprises at most 0.5 per cent of surface area, the length of stay was equal or greater than the average burn of the body, regardless of the latter's extent. That there is a distinct difference in healing time of chemical and thermal burns can be seen from Table IV. Here the average hospital stay for chemical burns was 16.1 days while the average for the whole group was 20.5 days. This is all the more impressive by the fact that chemical burns had an average degree of 1.67 while thermal burns had an average of 1.43.

TABLE V
REGIONS OF BODY BURNED

Hands	91	Chest	31
Legs	90	Feet	28
Forearms	67	Genitalia	27
Head and neck	64	Eyes	21
Thighs	40	Abdomen	20
Arms	34	Buttocks	11

The occurrence of infection delays the healing of burns in general. No first degree burns were found to be secondarily infected but the hospital stay for second degree infected burns was 26.1 days and of third degree infected burns 50.4 days. There were a total of seventy-one secondarily infected cases or 23 per cent of the entire group. Of these, thirty-seven were seen promptly on the day when the burn was incurred. That delayed treatment may be a factor in occurrence of infection may be seen from the fact that thirteen patients were seen after twenty-four hours, five after forty-eight hours, six after seventy-

TABLE VI
INFECTED BURNS

Days elapsed before seen	0	1	2	3	over 3
No. of patients	37	13	5	6	10

Total infected 71
Percentage 23

Degree	No.	Hospital Stay, Days
1st	0	
2nd	67	26.1
3rd	15	50.4

TABLE VII
INFECTED BURNS

Day after admission when infection developed	1	2	3	4	5
No. of patients	36	22	8	2	2

Duration of infection	Under 5 days	Over 5 days	Over 30 days
No. of patients	51	20	1

Average 4.1 days

two hours, and ten after three days or more. All infections were present either at the time of admission or developed by the fifth day as shown in Table VII. Of all the infected cases, fifty-one remained septic for five days or less, and only twenty remained septic longer. One patient remained infected for thirty days, but the average duration of infection was only 4.1 days.

Four of the third degree burns were skin grafted. This did not affect the hospital stay in these patients, but it did modify the cosmetic and functional results, as all were deep burns over joint surfaces. All of these grafts were performed since 1939, therefore, the percentage is not a true estimate of the number of patients deserving this form of treatment.

CONCLUSIONS

1. The present-day management of burns depends on prompt use of blood plasma for shock, careful débridement of the burn and the use of the sulfonamides in curbing infection. Early active and passive motion is encouraged in all patients.

2. A series of 308 military burns is analyzed occurring over a period of fourteen years, with a statistical evaluation of factors determining the results of healing.

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INITIAL TREATMENT OF TRAUMATIC WOUNDS

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IT is believed that a person receiving traumatic wounds in this day of modern surgical achievement should have the full benefit of a plastic repair promptly done under proper conditions by a surgeon capable of obtaining a minimum of deformity and disfigurement for his patients.

If such wounds are properly treated within a reasonable time of their incurrence, recovery will be hastened and the hazard to life from infection will be reduced. Deformity, disfigurement and blemishes while awaiting secondary plastic repair will be avoided. The pain, inconvenience, loss of time and expense of a second operation or a series of them will be averted. In case of injuries so complicated and extensive that secondary plastic operation is unavoidable, future surgery will be enhanced and a good final result will be assured.

Where immediately available, a capable plastic surgeon should be called to attend traumatic wounds likely to result in deformity or disfigurement. However, appreciable delay precludes a satisfactory end result and is dangerous to the life of the patient; hence *every* surgeon should become proficient in the repair of such wounds so as to leave the minimum of scar and distortion. He should preserve tissues readily available for secondary repair and use every judgment to avoid the need for additional surgery.

In the repair of wounds it is necessary for the surgeon to study them carefully in order to determine the anatomical disarrangement and the nature of the instrument causing the injury, as well as the complications likely to ensue. Proper records of all injuries should be kept as to how, when and where they were sustained. It therefore becomes obvious that a working classification of wounds must be adhered to. The following simple grouping is suggested:

1. Abrasions: mild, moderate or severe; small areas to extensive areas.

2. Wounds: incised, mild, moderate or severe.

3. Wounds: lacerated, mild, moderate or severe.

4. Wounds: contused, mild, moderate or severe.

5. Complications or variations of the above: penetrating certain areas, perforating others, amputating a member, dividing a lip, an ear, the tongue, an eyelid, nerves, arteries, tendons, evulsing a cartilage, a nail, etc.

Traumatic wounds about the face, head, arms, hands and feet are generally not given the degree of respect due them. An attempt is made for closure without the proper setting and without sufficient armamentarium to accomplish a proper operation. So often a wound looks innocent enough by observation and its full extent is not realized until its repair is in process and an adequate exploration reveals astounding complications. For instance, an apparent moderate scalp wound may very likely extend into a depressed fracture of the skull and in turn may have a foreign body penetrating the brain. (Such a case actually happened on this service recently.) Furthermore, such an innocent looking wound may be complicated by the division of important nerves or tendons.

Since the above is true and infection generally is so disastrous to all wounds, the following rules are recommended and are actually enforced at this hospital:

Any wound requiring sutures should be treated with the same respect as would be a major abdominal procedure so far as

aseptic set-up goes. If upon admission the patient's wounds are dressed and some information is available as to the nature of the wound, the dressing should not be disturbed until the operative procedure is in progress. Under no circumstances is a dressing to be removed outside of the surgical clinic, and there only after the surgeon has scrubbed his hands and covered his head with skull cap and mask. No person is to enter the operating room without having on cap, mask and gown, while the operation is being prepared for or is in progress. The surgeon and his assistants undergo the same preparation as for a major operation, donning operating pajamas, cap, and mask, afterward completing a full surgical scrub.

FIG. 1. Taken approximately one hour after patient was seriously injured in an automobile crash. Preoperative cleansing has been only partially accomplished. The ragged wound dividing lower lip extends to bone from left lower cuspid tooth to inferior border of mandible avulsing the soft tissues covering the mandible from the angle to the symphysis menti tearing the floor of the vestibule. The wounds of the upper lip and nose perforate into their respective cavities.

FIG. 2. Preoperative cleansing is practically complete. The tissue hook holds up the left portion of the lower lip.

The surgeon who is to cleanse the wounds puts on sterile gloves, and follows the procedure outlined below; the others get into sterile gowns and gloves and await the actual start of the operation. After an unsterile nurse or attendant cuts the bandages free, the entire wound area, including the wound, is cleansed of all dry blood with hydrogen peroxide solution Any necessary shaving is done with a sterile razor, followed by a thorough washing of the entire area with sterile-whipped white soap which is lavaged away with sterile water; the sponges used are held with the forceps throughout. The area is then dried and thoroughly cleansed with ether, and the skin antiseptic is applied to the entire area up to the wound edges. The surgeon now removes his gloves, and if indicated goes through the scrub procedure again, gets into sterile gown and gloves and the operation is ready to proceed. The patient is draped to expose with ease all wounds to be treated, and all except the first one are temporarily covered.

At this hospital 2 per cent procaine as local, or combined with nerve block, is used sparingly as the anesthesia of choice in the primary closure of traumatic wounds, and is done prior to the actual cleansing and exploration of the wound. The wound is now inspected and thoroughly searched for foreign bodies. If there is clotted blood and foreign matter such as dirt, glass, pieces of clothing, splinters of wood or hair present, such are removed; the instruments thus used are discarded, and the wound is lavaged with peroxide followed by irrigation with sterile saline until clean. The soiled drapes are discarded, the skin antiseptic is re-applied up to and including the skin edges, and new drapes are placed. If there is a tourniquet, it is now released and the necessary hemostasis is performed, the small grasps taken with mosquito forceps. The wound is thoroughly explored and a decision is reached as to how it will be repaired.

The repair of the wound is influenced by the extent of the damage, the degree of contamination, the time intervening since the injury and the demands of the situation. For instance, in the case of an ear almost completely excised, an extensive effort must be made to re-unite it so long as there is any evidence of viability. The longer the intervening time since injury, the simpler and more cautious the repair should be. A grossly contaminated wound indicates caution and minimal procedure, yet one must endeavor to obtain the minimal formation of cicatricial tissue, disfigurement and deformity.

The actual appearance of the wound influences the degree of surgery that may be undertaken. If the wound has had good first-aid care, for instance if a sterile pressure bandage has been used, it may reach the surgeon several hours after the injury and still be free of edema and weeping angry edges. On the other hand, a wound

Fig. 3.

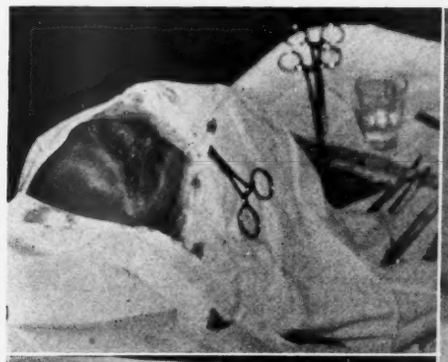

Fig. 4.

Fig. 5.

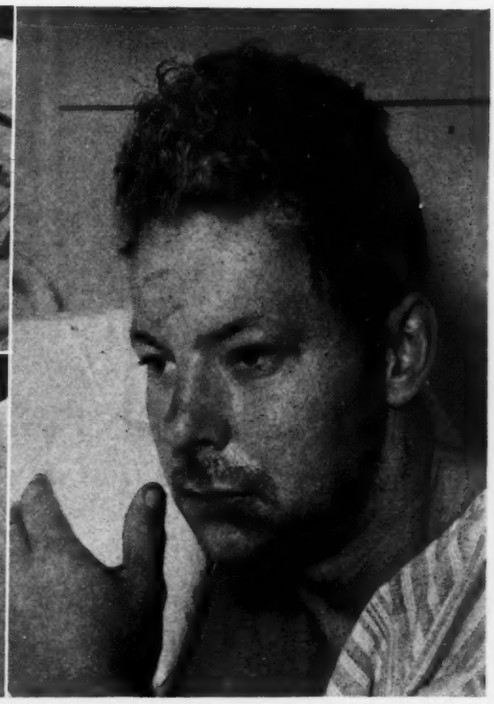

Fig. 3. Preoperative cleansing is complete, skin antiseptic has been applied and the wound has been draped.

Fig. 4. Surgery has been completed except for retention dressing.

Fig. 5. Seven days after primary surgery; all external sutures have been out for four days, the wound being held in close abutment with the collodion strips, which were reapplied for four additional days.

may present an unfavorable appearance in a short time if proper first-aid care has not been given. (Figs. 1 to 5.)

Aims of Operation. The aims are: (1) To re-establish anatomical relations and restore the features as nearly as possible to their original appearance; (2) to use methods that will give universally good results, doing scanty débridement where indicated to avoid the complication of infection; (3) to prepare and close the deeper structures so that equalization can be obtained in closing the skin and (4) to close the skin in such a manner that the resulting scar will be of skin level or slightly higher when all shrinkage has occurred.

A careful study of the wound edges with a magnifying glass or magnifying eye glasses will usually show slight irregularities of the edges at one or more places (notch on one side, projection on the other) left by imperfections of the sharp edge causing the wound. These irregularities will greatly aid in the exact re-approximation of the skin edges though they are usually drawn out of place by muscle pull. If a débridement of the wound edges is indicated, the above irregularities may be used in two or more ways: (1) by gentian violet lines drawn back from them and (2) by close sutures temporarily approximating the skin edges, followed by cross-marking the temporarily closed wound, and then by an excision of the indicated amount of skin, the final closure joining the cross-markings.

If a wound is in condition to be closed, it will usually withstand the necessary débridement. However, the débridement should always be as stingy as conditions will permit, eliminating shredded, devitalized muscle or dirt impregnated tissue when it can be removed without hazard to important nerves and vessels.

Hemostasis should be complete. Scant bites with small forceps are tied with very fine plain catgut or white silk. Sulfanilamide crystals are placed in grossly contaminated wounds and over the closure, and antitetanus gas gangrene prophylaxis is given whenever indicated. At times *x*-ray therapy is employed prophylactically. Re-approximation of the deeper tissues requires a careful rejoining of the structures in their proper anatomical relations, with the finest sutures practical for the tension placed upon them. Whenever a wound is in a region traversed by important nerves, function tests should be performed. If nerve function is lost, a definite effort should be made to demonstrate the severed nerves concerned and to repair them, provided, of course, that the wound is in operable condition. No. ooooo white silk on fine atraumatic needles is excellent for nerve repair. The same applies also to wounds in the area of tendons. However, if the wound shows any signs of infection or if the interval since injury is plus four hours, it is ordinarily best to leave the tendon closure for a secondary procedure.

GENERAL PRINCIPLES IN THE TREATMENT OF COMPLICATED WOUNDS

Wounds Likely to Result in "Trap Door" Scars. Incised wounds leaving the skin cut on a sloping bias are likely to result in "trap door" scars. If there is ample skin for excision of the two sloping edges without distorting the features and the wound is in good condition, it is thought advisable to excise the edges squarely. However, if such débridement of skin is not practical, the wound should be carefully closed from the deep structures out. Care is given to the subcuticular closure, and with the surgeon using numerous very fine black silk sutures, the skin is anchored all the way up the bias. A pressure dressing is sutured over the wound, and overlying this dressing a large sponge of cotton waste is placed and firmly held with stockinette bandage. Islands of skin scooped up or flaps raised with narrow, thin bases also have sloping edges. If these wounds are too large for simple excision and closure, they should be treated as outlined above and in addition the midportion should be anchored down with mattress sutures.

Fig. 6.

Fig. 7.

Fig. 8.

Fig. 9.

Fig. 10.

Fig. 11.

Figs. 6 to 11.

Fig. 6. Army nurse seriously injured in automobile wreck approximately seven hours prior to surgery. Photo taken twenty-four hours after surgery, showing the original dressing which consisted, from skin out, of scarlet red gauze, retention pad without sutures, forehead-nasal lead splint lined with sterile gauze, three bulky sponges of cotton waste, to which pressure is imparted by circular bandage of bias-cut stockinet. Fig. 7. Taken ten minutes after Figure 6. Gives some idea of the extent of injuries to head. The wound extending to bone from midforehead entered both nasal fossae and ended at tip of nose. The supporting structures of the nose were crushed and the soft tissues were avulsed laterally to cover eyes partially. A square cm. island of superficial tissues which was scooped from the left nasal dorsum to hang by a few shreds was used as a full thickness skin graft. The wound of the medial one-third left upper lid partially divided that structure. Attention is called to the relative absence of edema, as evidenced in Figures 7, 8 and 9, taken on consecutive days with reapplication of the large pressure dressings following Figures 7 and 8. The author believes the swelling from edema would have been enormous without a pressure technic. Fig. 10. Here on the third day all sutures except the intranasal sutures and those holding the skin graft on the side of the nose are removed. The sterile tension-relieving strips are used for a triple purpose: (a) to hold the wound edges in abutment (b) to hold pressure to the skin graft, and (c) to hold the severe compound fractured nose in alignment and conformity. Fig. 11. Final result of the primary operation.

Wounds with Opposing Edges of Unequal Length. Wounds in which the instrument cutting the skin took a wide uneven bite, or in curving wounds having surgical débridement (the wider the débridement, the greater the disproportion), the opposing edges must be equalized as to length. This can be done by taking an equalizing triangle of skin from one or both angles of the wound. (Figs. 6 to 11.)

Other More Difficult Wounds: Wounds with Extensive Skin Loss. All wounds with a loss of skin too extensive for approximation require immediate skin grafting when in operable condition. At this hospital free, transplanted, thick-split skin grafts on wounds as old as eight to ten hours, having had a proper pressure dressing as first aid, have taken in approximately 100 per cent. Thereby the patient is saved the distortion from cicatricial contracture and also a prolongation of hospitalization that would result from awaiting the otherwise unopposed skin edges to granulate in and scar over with the added hazard of infection. This same technic is used to cover over a guillotine loss of a portion of a finger, tip of the nose, tab of an ear, and results in saving, in the case of fingers, the length which would be lost by flap closure or in minimizing and preventing the hard, often painful, scar that would form if allowed to granulate in and scar over.

Wounds that divide the lip, the tongue, wall or walls of the nares, the eyelid or the external ear, when fresh and in good surgical condition, require complete plastic closure. This is done with careful scanty débridement and accurate fitting of the underlying, sutures, e.g., mucous membrane, cartilage, salivary and lacrimal ducts, muscles, etc., held with simple or mattress sutures of fine white silk. Care must be exercised in rejoining the opposing mucocutaneous junctions. The subcutaneous tissue and skin closure is cared for as under *details of technic.*

In parallel wounds too close together for separate outside suturing to obtain eversion of the edges, a double bite, tripple bite, etc., of the end-on mattress suture can be used and the return sweep of the needle passed under both or all of the wounds. Each wound can then receive its interrupted suturing with the retention suture encompassing all. Triangular wounds, or wounds that cross-complicate the repair, are harder to prepare and obtain eversion in, and the blood supply in the corners is likely to be tied off in the suturing and become gangrenous if care is not taken. The blood supply is likely to be cut off at the angles by the use of subcuticular stitches if special care is not taken to keep the bites small and thin. One end-on mattress suture is well placed where the point of the angle joins its notch in triangular wounds, but two placed at right angles near it will almost certainly result in its becoming gangrenous. Here interrupted sutures very close to the edge must be used and can be so placed that the point is somewhat forced into its notch. For the corners where two wounds cross, two end-on mattress sutures opposite each other joining the four corners make a good start, but preclude the use of other end-on mattress sutures in the close vicinity. Use of interrupted sutures straight through at right angles to the level of the skin will help with the eversion and full abutment of skin edges. Otherwise the treatment is as described below.

Details of Technic in Wound Repair. Wounds which do not extend completely through the skin are repaired by close approximation with fine sutures. However, any wound which goes through the base of the skin so as to gape, or which can be separated to reveal subcutaneous tissue, requires detailed repair. Otherwise, the base of the skin will separate, leaving a broad, thin area of poorly epithelialized scar.

Undercutting the Skin. In fresh, clean wounds free of early signs of infection, a slight undercutting of the skin, with removal of a lineal wedge of the subcutaneous tissue, which would otherwise tend to prop open the wound, is of a definite advantage

to the ultimate skin healing. This permits close, easy abutment of the opposing edges.

Subcuticular Sutures. The subcuticular sutures should close the base of the skin. The skin must be held in equalization while they are being placed. The equalization of the skin can be obtained as before described or by the use of fine tissue hooks held at the extremities of the wound by an assistant, beginning the interrupted subcuticular suturing near one angle, placing all sutures, clamping the ends to be tied later, then tying these sutures from the extremities toward the middle alternately. Then without the hooks a suture is placed at each angle to avoid its being puckered by being held in place with the hooks. The sutures used in the subcuticular closure must be fine, No. 000 or No. 00000 white silk or similar sized plain catgut on a half-circle, cutting needle (atraumatic needle preferable). Again, when these sutures are tied, the skin is actually approximated with some eversion.

FIG. 12. FIG. 13. FIG. 14.

FIG. 15. FIG. 16. FIG. 17.

For descriptive legend see page 239.

Skin Closure. The skin sutures require exacting care. The edges should be everted evenly with the highest eversion at the center of the wound. The sutures should be so placed that opposing edges are caught equidistant from the angles at the same depth from side to side and so placed that the entire depth of the skin is abutted for its full thickness. The sutures should actually stretch the depth of the opposing edges. The most important feature of the skin sutures is that they be placed close to the skin edge so that, if they cut, the resulting scars will not be large ones and will be

easily repairable. The sutures must be fine, of nonirritating material and not tied too tightly. It is unnecessary for the suture to

suture, the surgeon crosses the needle underneath the wound line and out at right angles to the skin at an equal distance. The

Fig. 18.

Fig. 19.

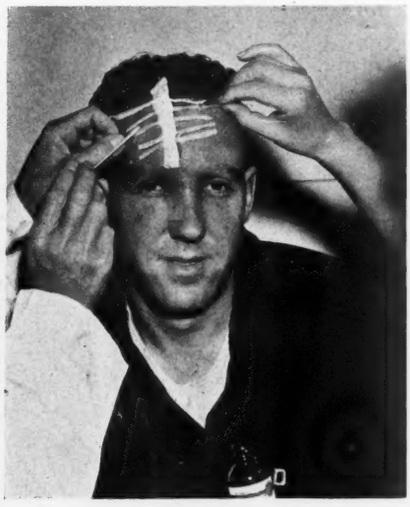

Fig. 20.

Fig. 21.

Fig. 22.

Fig. 23.

For descriptive legend see page 239.

be further away from the skin edge than the thickness of the skin in the area being repaired. Every precaution is taken to avoid adding trauma to the already injured skin.

End-on Sutures. The end-on mattress suture is placed through the edge of the skin and sloped to whatever degree necessary to obtain the desired amount of eversion in the wound, and out on the other edge at exactly the same depth and angle. At the back-sweep while lifting on the suture so as to stretch the skin away from its base, going through the skin at right angles just beyond the emergence of the knot is tied without tension, no effort being made forcibly to abut the skin edges. Even though the top edge separates slightly, this suture should not be tight. In the placement of these sutures, approximately one for each one-fourth inch, the fine tissue hooks above mentioned aid in lineal equalization of the skin edges and the gentian violet equalization marks above mentioned may be used. The same caution should be taken not to hold the angles in pucker while placing the wound angle sutures.

Interrupted Suture at Right Angle. Interspaced midway between each end-on suture, an interrupted suture is placed

Fig. 24. Fig. 25.

Fig. 26. Fig. 27.

Figs. 12 to 27.

Illustrations showing the postoperative care following repair by modified "Poulard's" Method, of an old adherent scar in a depressed frontal fracture. This postoperative care is used routinely by the author in traumatic and many other wounds. Figs. 12 and 13. Before operation. Figs. 14 to 17. Represent a modification of a pressure technic originally suggested to author by Dr. James Barrett Brown. Fig. 14. The complete dressing. Fig. 15. The small surgical pad sutured over wound to concentrate pressure to the wound. Fig. 16. Showing the wound overlayed with scarlet red gauze. Fig. 17. Shows all external sutures and the long sponge-holding sutures. (Never tied tightly.) Fig. 18. The end-on sutures have been removed. Fig. 19. Bandage strips anchored to alternate sides with collodion. Fig. 20. Surgeon and assistant pull alternate strips and glue them down across a strip of gauze over scarlet red gauze. Fig. 21. The collodion strip ends are tagged with adhesive. Fig. 22. Pressure is added to the wound site with adhesive over folded gauze. Fig. 23. The third day dressing. All sutures are out. Fig. 24. The bandage strips are glued to the skin on alternating sides right up to the skin edge. Fig. 25. The strips have been fastened across, as above. Fig. 26 and 27. Show the after results of the one operation.

which goes through the skin at right angles and back from the wound edge on a level with the back bar of the end-on suture. This suture is tied with the knot directly on top of the wound and an effort is made to abut the skin edges without tension.

Shallow Wound Sealing Sutures. A third row of sutures is placed equidistant between the above two types of sutures and is of the finest available silk, No. 000 or No. 00000 black, threaded on a very fine half-curved eye needle and placed sloping very close to the surface, and to the edge of the skin. It is tied quite firmly and used to seal the outer edge. Complete coverage of the wound by skin is essential. The wound and area now are thoroughly cleansed of all dry blood with peroxide and saline.

Retention Sutures. The retention sutures, involving the use of size D black silk or horsehair suture on a noncutting, fine, triangular, pointed needle, one inch long, half-curved, are placed back approximately one-half inch from the skin edge where practical, and again go directly through the skin and out at right angles, being placed at about one-half inch distance lineally. These sutures are left long. (Figs. 12 to 27.)

Dressing the Sutured Wound. With the wound entirely cleansed of dry blood, scarlet red 5 per cent ointment impregnated in three-inch fine mesh bandage gauze is laid over the wound. Over this is placed a row of cotton waste in gauze, of sufficient thickness to hold the retention sutures from their tendency to pull toward the wound. The retention sutures are tied over this roll with caution against tying them too tight, for tension here would be disastrous. Gauze is then placed around the roll to convert the dressing into an oval pack. Then a large sponge made of cotton waste is placed over the entire area even though it may be necessary to cover one or both eyes, and a pressure bandage of diagonally cut stockinette is applied to form and hold pressure. The aim of this type of dressing is to avoid stagnation in the wound area with resultant edema formation, and thus to aid the return circulation.

First Change of Dressing. The dressing is left on for twenty-four to forty-eight hours, depending upon the comfort of the patient. It is then removed carefully with saline soaking used if it is stuck to the wound. The retention sutures are cut close to the skin on one side and removed. The scarlet red dressing is soaked off with peroxide. Ordinarily, it is found that the retention sutures have served as drains for the wound as evidenced by dry blood at their points of emergence. The wound and the surrounding areas are found to be free from edema and swelling and the wound edges entirely free of dried serum or other wedge-forming material. The wound is washed with peroxide and is painted with Scott's solution which is allowed to dry. All end-on sutures are removed at this dressing if forty-eight hours have passed, or after twenty-four hours if such sutures appear to be cutting.

Collodion Tension Relieving Strips. A three-thickness fold of scarlet red impregnated bandage gauze is laid over the suture line, just wide enough to cover it, and over this a small strip of gauze. Using collodion as glue, sterile strips of bandage one-eighth inch wide are fastened to the skin on alternate sides crossing the wound, close to the gauze. Using a hand hair dryer to speed drying, the dressing surgeon pulls on a strip on one side with his left hand while an assistant pulls on the next strip on the opposite side with sufficient force to take all tension from the suture line. (Figs. 19 to 25.) All strips are glued into place.* In this manner the scarlet red is held firmly to the wound edge and all tension is removed from the sutures. On top of this a firm sterile gauze dressing is placed with adhesive strips at right angles to the wound in such a manner as to reinforce the pressure in the direction of the wound edges.

* I devised this method of relieving the wound of the normal skin tension (tendency of the wound to separate) approximately four years ago and used it since with a great deal of success.

Second Change of Dressing. When forty-eight to seventy-two hours have elapsed from the time of operation, this last dressing is removed. All remaining sutures are taken out and the tension-relieving collodion strips are again applied, from well back of the wound up to the very wound edge. (Figs. 24 and 25.) While alternate strips are pulled on with just sufficient force to relieve all tension from the wound, the glueing process is completed. A sterile gauze pad is laid over the wound edge, and adhesive strips are laid across the pad in the same direction, thus covering the extremes of the collodion strips. This dressing remains until the eighth postoperative day. Quite often all sutures are removed twenty-four to forty-eight hours after surgery and the tension relieving collodion strips put in place; these serve to hold the wound in approximation without untoward effect. However, where adequate pressure is held on the wound area, and undue tension is thus kept from the sutures with the strips, there is seldom inclination for the sutures to mark. Allowing them to remain for a longer interval—a total of three or four days—is believed to be safer. It is only when slight edema occurs or the patient has acne, has a very irritable skin, or has an abrasion complicating the wound, that earlier removal of the sutures seems indicated. When the sutures are found to be too tight, they are removed and the skin is held in close approximation with the collodion strips. Even if all sutures have to be removed at the twenty-four hour dressing, the tension relieving strips hold the skin in close abutment without tension, and also tend to hold the edges level in depth, and the final result is seldom any the worse for it. I know of no other safe means of so early a total removal of external sutures. The strips are sterile and the wound is not sealed with the collodion.

CONCLUSIONS

1. Traumatic wounds should have immediate plastic repair in order to obtain the minimum of deformity and disfigurement.
2. For wounds likely to result in gross disfigurement a plastic surgeon, if immediately available, should be called.
3. Since delay is ruinous to the end result and dangerous to the life of the patient, every surgeon should become proficient in the initial plastic repair of traumatic wounds in order to reduce the incidence of scar formation and disfigurement.
4. Regardless of the prior contamination to the injury, the strictest asepsis is required in the surgical repair, with full protection from respiratory contamination.
5. The collodion tension-relieving strips are a definite aid in obtaining a minimal scar.

OPERATING ROOM DEATHS*

A STUDY OF TWENTY-THREE CONSECUTIVE CASES IN WHICH AUTOPSIES WERE PERFORMED

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THERE is no experience in medicine more distressing than that of an "operating room death" and this is especially true when the death is sudden and unexpected. With this thought in mind we have studied twenty-three consecutive cases of operating room deaths in which autopsies were performed, covering a period of ten years from 1931 to 1940 in the Royal Victoria Hospital. Excluded from this series are all neurosurgical cases save one which was included because of close similarity to another case in this series. All patients were under anesthesia whether it was local, spinal or general, and all patients were either undergoing operation or had undergone operation and had not yet been returned to the ward.

In studying these cases an attempt has been made to find both the underlying and the immediate causes of death, and if possible to put them both on a physiological as well as an anatomical basis. In a limited way certain results might be obtained from such a study: (1) a better understanding of just what constitutes a definite surgical and anesthetic risk; (2) a more rational basis from which to choose the most appropriate anesthetic agent; and (3) a better understanding as to the preoperative care of those patients who constitute definite risks.

Of course, there is rarely a single cause for death. Usually a combination of factors is present, all of which contribute their share to the final outcome. Therefore, these cases have been grouped according to the underlying mechanisms concerned.

These are the "atria mortis" which according to Oertel was the term used by the ancient physicians to denote the cerebral, respiratory and cardiac types of death. Accessory factors having any bearing on the final outcome are included in Table II.

TABLE I
TWENTY-THREE OPERATING ROOM FATALITIES

Predominating Causes of Death	No. of Cases
I. Cardiac	3
II. Asphyxia	5
III. Shock	7
IV. "Pleural shock"	2
V. Air embolism	2
VI. Anesthesia	4
Total	23

CASE REPORTS

In the interest of brevity only representative cases from each group are presented in full. It is immediately apparent that many different mechanisms are often at play in each case. These mechanisms and other factors of importance are presented in the form of a discussion at the end of the presentation of case reports. In the consideration of these cases it should be kept in mind that in the ten-year period from which these cases were taken there has been much improvement in the administration of anesthesia. In the light of present knowledge, anesthetic agents used in certain cases several years ago, would not be used in those same instances now.

I. Cardiac. In the cardiac group of three cases there were two cases of aortic stenosis with insufficiency and one case of hypertensive cardiovascular disease with aortic insufficiency. This last patient had a blood pressure of 150/80 and was con-

* From the Department of Surgery, Royal Victoria Hospital, Montreal.

TABLE II

Case No.	Sex	Age	Operation	Diagnosis	Cause of Death	Contributory Cause	Anesthetic Employed	Anesthetic of Choice
I	M	18	Appendectomy	Chronic appendicitis	Aortic stenosis	.....	Ether	1. Cyclopropane 2. Ether
II	M	54	Herniotomy	Inguinal hernia	Cardiac decompensation	Spinal anesthesia	Pontocaine (spinal)	Local and gas
III	F	22	Craniotomy	Glioma of cerebellum	Aortic, Mitral, Tricuspid } stenosis	.....	Local and ether	1. Local 2. Ether
IV	M	52	Thoracotomy	Carcinoma of bronchus	Aspiration of pus	.....	Chloroform and N_2O	1. Cyclopropane 2. N_2O
V	M	75	Incision and drainage abscess of neck	Abscess of neck	Edema of glottis	Carotid sinus reflex	Local	Local
VI	F	16	Thoracotomy	Malignant thymoma	Compression of trachea	Avertin and gas anesthesia	Avertin and N_2O	Cyclopropane (intratracheal)
VII	M	42	Thyroidectomy	Lymphosarcoma of thyroid	Compression of trachea	.....	Cyclopropane (intratracheal)	Cyclopropane (intratracheal)
VIII	M	50	Second stage thoracoplasty	Pulmonary tuberculosis	Decreased vital capacity	1. Brown atrophy of heart 2. N_2O anesthesia	N_2O	1. Cyclopropane 2. Spinal
IX	F	16	Pneumonectomy	Lung abscess	Pleural shock?	Status thymicolymphaticus?	Local and N_2O	1. Cyclopropane 2. Spinal 3. Local
X	M	56	Pneumonectomy	Lung abscess	Pleural shock?	Status thymicolymphaticus?	Local	1. Cyclopropane 2. Spinal 3. Local
XI	M	41	Repair of perforated ulcer	Perforated peptic ulcer	Shock	Prolonged recumbency—"sublethal shock"	Local	Local
XII	M	52	Repair of perforated ulcer	Perforated peptic ulcer	Shock	Spinal anesthesia	Spinal	1. Spinal 2. Perhaps local
XIII	M	28	Pyelotomy for stone	Abscess left hip; nephrolithiasis	Shock	Prolonged recumbency—"sublethal shock"	1. Avertin and gas 2. Ether	Cyclopropane
XIV	M	19	Appendectomy	Appendiceal abscess and pylephlebitis	Shock	Severe toxemia	Gas and ether	Cyclopropane
XV	F	49	Appendectomy	Perforated appendicitis; peritonitis	Shock	.....	N_2O and ether	1. Spinal 2. Local and gas
XVI	M	57	Cholecystojejunostomy	Carcinoma of head of pancreas obs. jaundice	Shock	Spinal anesthesia	Spinal	Spinal
XVII	M	37	Gastrostomy	Bleeding peptic ulcer	Shock	.....	Spinal	1. Loacl 2. Cyclopropane 3. Spinal
XVIII	M	35	Pneumonectomy	Bronchiectasis	Air embolism	.....	N_2O (intratracheal)	Cyclopropane (intratracheal)
XIX	M	23	Lobectomy	Bronchiectasis	Air embolism	.....	Chloroform and N_2O	Cyclopropane (intratracheal)
XX	F	34	Delivery	Pregnancy	Chloroform	.....	Chloroform	1. Cyclopropane 2. Ether
XXI	F	38	Appendectomy	Appendicitis; localized peritonitis	Gas and ether	Unknown factors	N_2O and ether	1. Spinal 2. Ether
XXII	M	64	Exploratory	Adenocarcinoma of sigmoid	Spinal anesthesia	.....	Spinal	Spinal
XXIII	M	63	Gastrostomy	Myosarcoma of tongue	Spinal anesthesia	Aspiration pneumonia	Spinal	Local

sidered to be decompensated. Each of the first two patients, although compensated, had a blood pressure of 80/60. In all three cases death was rather rapid and unexpected.

Case I. A male, age eighteen, with acute appendicitis, had been known for years to have heart disease. There was cardiac enlargement, aortic systolic and diastolic murmurs and a blood-pressure of 80/60, but there was no evidence of decompensation. Operation was performed under ether anesthesia for a period of forty-five minutes. He breathed poorly throughout. Respirations were 30 to 40 per minute, and pulse was 110 to 120. As the operation came to a close, both respiration and pulse ceased quite suddenly. The usual methods of resuscitation were tried without avail.

At autopsy the heart was quite large, weighing 670 Gm. and there was a well marked aortic stenosis superimposed on a bicuspid aortic valve. The aorta was small, measuring only 3.5 cm. in circumference.

Comment. The choice of anesthesia was considered to be a good one, as it was possible to give an excess of oxygen along with the ether. However, cyclopropane would have been a better choice, and perhaps the operation could have been performed even under a local anesthetic.

Case II. A male, age fifty-four, with a right indirect inguinal hernia, had hypertensive cardiovascular disease of at least five years' known duration. There was a history of dyspnea on exertion and ankle edema, and physical examination revealed cardiac enlargement, aortic, systolic and diastolic murmurs, and a blood pressure of 120/80.

Two to three minutes after the injection of spinal anesthesia the blood pressure dropped to zero and the patient expired. At autopsy the premortem diagnosis of hypertensive cardiovascular disease was confirmed.

Comment. The fatality in this case may be considered as due to a questionable choice of an anesthetic in a poor risk patient since the greatest drop in blood pressure usually occurs within the first fifteen minutes of spinal anesthesia. In this case local and gas would have been the anesthesia of choice. Local anesthesia alone was not used as the hernia was a large one, and an attempt at fascial repair was going to be made. In this case the cardiovascular system was already impaired, and oxygenation of the blood was being carried out at a great expense of energy and with only a small margin of safety.

II. Asphyxia. Case V. A male, age seventy-five, was admitted to the hospital *in extremis*. There was considerable respiratory distress and he gave the history of having been unable to swallow some hours prior to admission. There was a phlegmon on the right side of his neck. He was given oxygen by mask in the ward, and then later taken to the operating-room where incision and drainage were carried out under local anesthesia. During the operation, respirations gradually became slower and oxygen was then given by intratracheal catheter but the respirations finally ceased. There had been no struggling at any time during the operation.

At autopsy an abscess was found behind the left tonsil. There was arteriosclerosis, some cardiac enlargement and dilatation, early bronchopneumonia of the left lower lobe and a purulent bronchitis.

Comment. It was believed that this patient died from asphyxia, the result of massive edema of the glottis. A gradual slowing of the respirations with deepening cyanosis, as present in this case, is characteristic of respiratory failure with terminal exhaustion of the higher centers. However, the fact that death occurred without struggling, although only local anesthesia was used, brings up the question of syncope secondary to a possible carotid sinus effect, which has been mentioned in the literature in similar cases.

In another case, one of an esophageal carcinoma on whom permission for autopsy was refused, death occurred a short time after an incision had been made in the neck. Just before death it had been noted that when the incision was made in the neck, the pulse became slow and strong. The operation was stopped for a moment and the pulse then returned to normal. On

continuing the operation, the patient died. This man was fifty-eight years old and his blood pressure was 158/98. There was no evidence of cardiac decompensation. However, there was a history suggestive of angina pectoris. Examination of the heart had revealed a loud aortic systolic murmur transmitted to the neck vessels.

Case vi. A female, age sixteen, had a malignant thymoma with invasion of the sternum and marked secondary compression of the trachea. The operation was performed under avertin and gas anesthesia. From the start of the operation there was extreme difficulty in breathing; respirations were shallow and the patient cyanotic. After resection of the first rib, it was thought wise not to proceed further as respirations were becoming increasingly weaker. Intratracheal oxygen was tried but the patient expired.

At autopsy the trachea was found flattened and there was moderate pulmonary edema and marked passive congestion of the viscera.

Comment. In this case, in view of the respiratory embarrassment, avertin-gas anesthesia was definitely contraindicated. Cyclopropane, which was not available in the year this operation was performed, and oxygen administered by intratracheal catheter would have been the anesthesia of choice.

The marked slowing of the respiratory rate seen in the above case is due to the Hering-Brauer reflex. The marked pulmonary edema so often a feature in these cases is thought by some to be caused by the aspirating effect of a negative alveolar pressure during inspiration. If so, the mechanism of its production differs from that of the pulmonary edema seen in shock, which is probably due to increased permeability of capillary endothelium. However, anoxia in itself causes an increase in the permeability of capillary membranes. Perhaps in both of these instances anoxia is of great importance in the causation of pulmonary edema.

III. "Pleural Shock." Case ix. A female, age sixteen, well nourished, was admitted with a lung abscess. Physical examination was essentially negative except for the abscess in the right lower lobe. The operation was carried out under nitrous oxide anesthesia with the patient in a sitting position. As the pleural adhesions were being cut a vessel was opened by the cautery, which bled for only a few seconds before it was stopped by coagulation around the area. At this moment her heart suddenly stopped beating although respirations carried on for a minute or two.

At autopsy the patient appeared healthy and slightly obese. The mesenteric glands were large. A moderate-sized abscess was found in the right lower lobe.

Comment. If the death had been due to gas anesthesia, one would expect respiratory failure to precede failure of the circulation. Was death due to air embolism? No pathological evidence was found to substantiate this belief. Was this a case of status thymicolymphaticus? Just what is the so-called "pleural shock"? An attempt to answer these questions will be made in the discussion which follows.

Case x. This case was similar to the previous one in that cautery pneumonectomy was again being carried out for lung abscess. A male, age fifty-six, was operated upon under local anesthesia which was not altogether satisfactory as the patient experienced some pain during the use of the cautery. Quite suddenly, when about a third of the way through the operation, the patient seemed to go into syncope. He lost consciousness, the respirations became shallow and the skin cyanotic. The respirations then ceased and shortly afterward the heart stopped beating.

Autopsy showed the body to be well developed and slightly obese. The heart weighed 330 Gm. and there was interstitial fibrosis along with some microscopic hypertrophy of the muscle fibers. There were no other findings of note.

Comment. This case is interesting in that interstitial fibrosis of the myocardium is frequently found in cases diagnosed as having status thymicolymphaticus, and it is considered by some as one of the characteristic, although not constant, features of the syndrome.

IV. Shock. Case xii. A male, age fifty-two, was admitted to the hospital with a perforated gastric ulcer of some hours' duration. Spinal anesthesia was given as the patient was known to have bilateral pulmonary tuberculosis. An urgent case, he was an extremely poor risk with a preoperative blood pressure of 90/64 and a pulse of 140. The operation lasted thirty-five minutes and the patient died some forty minutes later in the operating room. He had not been moved back to the ward because of his critical condition.

At autopsy the body was well nourished. The positive findings were limited to the lungs and abdomen. The lungs were heavy and voluminous, weighing 520 and 610 Gm. and microscopic study showed edema and dependent congestion. There was a left-sided hydrothorax of 400 cc. The perforated ulcer was found and the surrounding peritoneum was seen to be covered with a fibrinous exudate.

Comment. Obviously, this case is one of shock due to the overwhelming reaction caused by perforation of a peptic ulcer. The use of spinal anesthesia in the presence of such low blood pressure and even the trauma of surgery itself had some bearing on the final outcome, but their effect must have been very minor as compared to the shock resulting from intestinal perforation.

Case xiii. A male, age twenty-eight, had developed osteomyelitis of the left hip and femur as the result of a gunshot wound in the left hip. The bladder had also been perforated at the time of injury and there was a vesical sinus draining through the hip wound. His hospitalization was a long one and as the result of urinary infection together with prolonged recumbency and stasis in the urinary tract, he developed nephrolithiasis. A pyelotomy was performed under avertin and ether anesthesia. His condition which was rather poor at the start became rapidly worse. The pulse was rapid and thready. While the wound was being closed he stopped breathing and expired.

At autopsy he was seen to be poorly nourished. The right side of the heart was moderately dilated. The viscera were congested and the lungs showed bronchopneumonia and congestion at both bases. There was also a pyonephrosis (right) with bilateral septic renal infarcts. There was exudative purulent osteomyelitis of the left hip and femur.

Comment. Death in this instance was due primarily to shock to which a weakened physical state secondary to prolonged hospitalization must have played an important part. It might also be well at this point to mention the importance of psychic factors in regard to operative risks. It is believed that psychic trauma will also bring on a shock state due to the bombardment of the neurovascular apparatus with nervous impulses. In this particular case, the patient, due to sepsis and prolonged hospitalization, had deteriorated considerably from the standpoint of morale. It was noted on frequent occasions that even the giving of a hypodermic resulted in considerable pain and mental anguish. The patient also exhibited fear and extreme nervousness prior to operation. Quite possibly the nervous element in this case played an important rôle in producing his shock state as found at operation.

V. Air Embolism. Cases xviii and xix. Both of these cases were lobectomies for bronchiectasis. In one of them the right pulmonary vein was cut, in the other, four or five small branches of the pulmonary vein.

Autopsy findings in both cases were characteristic. There was frothy blood in the heart, air in both the coronary and cerebral arteries, and petechial hemorrhages in the cerebral cortex and subarachnoid space.

VI. Anesthesia. Anesthetics *per se* have accounted for only a relatively small number of these deaths. In two of the twenty-three cases spinal anesthesia was held to be the cause of death, in one of them chloroform was held responsible and in the other ether was the predominating factor.

Case xx. A female, age thirty-four, healthy, para iv, gravida v, prior to delivery had been given 3 gr. of nembutal. She was given a light chloroform anesthesia, not exceeding five minutes. Labor was short and spontaneous and the blood loss small. While the placenta was being delivered, maternal respirations became labored, she became deeply cyanosed, and in a very

short time pulseless. She died twenty minutes postpartum.

At autopsy there were focal degenerative changes in the liver (central necrosis). There were petechial hemorrhages in the liver, gastrointestinal tract, renal pelves and bladder. The right side of the heart was dilated and there was marked cloudy swelling of the heart and viscera.

Case xxi. A male, age thirty-eight, was admitted with acute appendicitis and localized peritonitis. On admission his temperature was 102°F., pulse 136, respirations 26, blood-pressure 140/90 and white blood cells 17,500. Appendectomy with drainage was carried out under nitrous oxide and ether anesthesia which lasted for one hour and fifteen minutes. During the removal of the appendix the patient developed marked tremors, first of the upper half of the body and later extending to the whole body. These later progressed to convulsive seizures which apparently became gradually less severe. By the time the operation was finished, the respirations were irregular and there were breath holding spells during which he would get quite cyanotic.

At autopsy the body was considered to be well developed. The trachea was edematous and there was marked pulmonary edema and congestion. The left chest contained 50 cc. of fluid. There was congestion of the bowel and beginning peritonitis in the right lower quadrant.

Comment. This patient who was operated upon on a very hot day in August, represents one of the so-called "ether convulsions." As is usually the case, the patient was very sick with evidence of toxemia.

Case xxii. A male, age sixty-four, lapsed into a semiconscious state a few minutes after having been given spinal pontocaine. He was taken into the operating room where an intravenous injection was started. It was then decided to go on with the operation. However, as soon as the incision was made the respirations ceased. The usual restorative measures were tried, including massage of the heart, which kept the heart beating for only a short while.

At autopsy nothing in particular was found to explain the death, so it must be considered as due to respiratory failure on an anesthetic basis.

Case xxiii. This is a case of a male, age sixty-three, with a myosarcoma of the tongue of nine years' duration on whom a gastrostomy had been planned. At the time of operation the patient was slightly dyspneic and propped up in bed. He was given pontocaine spinal anesthesia with a resulting anesthetic level up to the fourth dorsal vertebra. Shortly afterward respirations ceased and he became unconscious. Adrenalin was given along with artificial respiration. An airway was then inserted. Asphyxia had resulted as the intercostal muscles were thrown out of action in a man whose respiratory physiology was already impaired. He was then kept in good condition during the operation by oxygen and carbon dioxide under positive pressure. When this was discontinued prior to return to the ward, he again underwent respiratory failure, which this time did not respond to treatment.

At autopsy the lungs were found to be voluminous and heavy, weighing 715 and 1,065 Gm. There was moderate pulmonary edema. Abundant fat globules were also found in the bronchi and alveoli, both grossly and microscopically, and this was associated with an exudative and productive pneumonia.

Comment. Obviously, this is a case which should have been done under local anesthesia. The tumor of the tongue causing a partially obstructed airway, and the diffuse lung infection, supposedly an aspiration pneumonia, contributed strongly to the final outcome.

DISCUSSION

Anoxia. In searching for some feature common to these cases of operating room deaths, it became immediately apparent that in all but a few of them asphyxia or oxygen deprivation of the tissues was a factor of the greatest importance. In these cases the progression of oxygen want or anoxia could be followed clinically, and at autopsy the effect of this anoxia could readily be seen.

Because we believe that anoxia may be considered the common denominator of many of our cases, a short résumé of this subject has been undertaken.

By definition, when the tissues fail to receive an adequate supply of oxygen, we

say there is anoxia, or oxygen want. This may come about in one of several different ways, and these Barcroft has separated into three groups: (1) Anoxic anoxia, which is that state resulting from defective oxygenation of the blood; (2) anemic anoxia, in which there is a lack of or inactivation of hemoglobin; (3) stagnant anoxia, which is due to slowing of the circulation through the capillaries and smaller blood vessels. A fourth subdivision was later added, by Peters and Van Slyke, (4) that of 4 histotoxic anoxia, in which the tissue cells are inactivated or drugged so that they cannot utilize the available oxygen.

It is obvious that any of these several mechanisms may lead to asphyxia. However, it is usually a combination of several or even all of these types which results in serious complications. For example, while emphysema will result in a degree of anoxic anoxia due to *decrease in alveolar aeration*, secondary anemia would result in a degree of anemic anoxia, surgical shock in stagnant anoxia, and preoperative medication such as nembutal and morphine in histotoxic anoxia. If all four of these conditions were present at the same time, as is conceivable during the course of an operation, the sum total might easily be more than the patient could stand.

McClure et al.[1] have discussed this subject and the effect of the various anesthetic agents in respect to anoxia. A few of their conclusions are of interest. For example, they point out that 80 to 95 per cent concentration of nitrous oxide in the blood is necessary for good anesthesia. However, this leaves less oxygen than necessary for maintenance of an adequate oxygen tension in the blood. As a result, therefore, anoxic anoxia is produced, first by a reduction of arterial oxygen tension, and then latter by depression of the respiratory center. On the other hand, the action of avertin is different in that it produces anoxic anoxia through respiratory depression and then by circulatory depression a stagnant anoxia. However, the most widespread effect is *probably* that of the barbiturates. They are known to act through the di-encephalon, and they have both sedative and hypnotic action. There is an initial circulatory depression, thus a stagnant anoxia, then later respiratory depression with resulting anoxic anoxia. However, the most important effect is on the cellular respiration, histotoxic anoxia. Finally, in spinal anesthesia a degree of circulatory depression may result from paralysis of the vasoconstrictors in anesthetized areas and with this there comes a stagnant anoxia. But it is probable that most of the fatal accidents due to spinal anesthesia are secondary to paralysis of the phrenic mechanism, the intercostals, or of the respiratory center.

It follows, therefore, that those cases which exhibit a relative anoxia prior to operation, no matter what the cause, are operative risks. This is because the anoxia already existent is almost certainly to be made worse by the addition of other types of anoxia through the use of preoperative medication and anesthesia, and through shock due to various reasons such as psychic trauma or surgical trauma secondary to the operation itself.

The discussion of the following seven subjects is of importance as they have bearing on the various causes of death in the different cases presented in the case reports.

1. *Aortic Stenosis.* Aortic stenosis is now well known to be a cause of sudden death. Marvin and Sullivan,[2] in 1935, reviewed this subject and out of 228 cases of aortic stenosis in which autopsies were performed they found seventeen cases of sudden death. The mechanism concerned is a moot point. The available evidence accumulated by them did not support the belief that syncope was due to cerebral anemia dependent upon inability to force blood through the stenotic aortic orifice. They believed that it was due most probably to a hyperactivity of the carotid sinus reflex or some reflex involving the same central and efferent pathways. As for the aortic stenosis found in this case, it was not

definitely proved to be rheumatic in origin nor was there any history of rheumatic fever. Quite possibly, the congenital bicuspid valve played an important part in its etiology.

2. *Carotid Sinus Reflex.* The carotid sinus reflex as a cause of sudden death in surgical cases has been mentioned a number of times in the literature. Cohn,[3] Downs,[4] and Rovenstine and Cullen[5] mention that in their experience "sudden deaths following incision and drainage of abscesses in the neck are not rare." The anesthetic agents, nitrous oxide and chloroform, certain barbiturates, avertin and morphine, all have been found experimentally to sensitize the carotid sinus (Downs[4] and Rovenstine[5]).

According to Soma Weiss,[6] 70 to 78 per cent of those people with hypertensive cardiovascular disease or advanced arteriosclerosis have a hyperactive carotid sinus reflex. This is interesting in view of the two cases presented above, both of whom were well along in years and showed evidences of arteriosclerotic changes. Robinson[7] and Weiss et al.[8] have written thorough discussions of the syndrome of the hyperactive carotid sinus reflex.

3. "*Pleural Shock.*" About "pleural shock" little is known and very little has been written. It is a term used to denote cases of unexplained sudden death occurring during the course of thoracentesis or other surgical procedures in which the pleura is irritated. Two theories have been suggested in explanation of this occasional but yet all too frequent catastrophe (Graham[9]). The first is that of cerebral air embolism, and the second is that which presupposes some unknown pleural reflex, in the nature of a vasovagal reflex. Frequently, when the pleura is irritated experimentally, usually an inflamed pleura, there is an associated marked fall in the blood pressure. This reflex is assumed to be transmitted through the vagus nerve. More credence, however, has been placed in the theory of cerebral air embolism. It has been shown that very small amounts of air injected rapidly into the pulmonary veins will occasionally cause death, whereas much larger amounts injected into a systemic vein will have no harmful effect.

4. *Status Thymicolymphaticus.* Another interesting subject which is of importance as far as this paper is concerned is that of status thymicolymphaticus. Death in several of the above cases remains unexplained and as they presented several characteristics suggestive of this syndrome, this summary is included.

Although it was the conclusion of a committee investigating status lymphaticus in the British Isles[10] that there was "no evidence that the so-called 'status thymicolymphaticus' has any existence as a pathological entity," nevertheless that there is such a diathesis is commonly held and that such cases are subject to sudden and unexplained death from what would appear to be trivial causes is a common observation. Symmers[11] found 249 cases out of 4,000 autopsies in Bellevue Hospital, New York, or 6.2 per cent of all cases. They came from all races in a proportion of males to females of 6:1. He found that a combination of hereditary constitutional anomalies may be found including: (1) certain peculiarities of bodily configuration; (2) preservation or even hyperplasia of the thymus at an age when involution might be expected; (3) hyperplasia of lymphatic tissue in spleen, intestines and elsewhere; (4) changes in hair distribution; (5) hypoplasia of the vascular system. Michael[12] believes that certain cases of operative death can be explained on this basis.

5. *Shock.* Shock forms by far the largest group of postoperative deaths, and it also accounts for the largest number of operative deaths. It is the main problem which both the anesthetist and surgeon have to contend with. Its causes are many and complex and its management is an urgent one. Its primary effect is that of a stagnant anoxia, and the pathology of shock is basically similar to the pathology of anoxia, due to whatever cause.

Briefly these changes consist of capillary dilatation with occasional small perivascular extravasations of blood. The viscera show passive congestion, and the lungs as a rule show pulmonary edema. Sometimes a diffuse hemorrhagic infiltration is present throughout the lung parenchyma. Pulmonary edema evidently is dependent upon the duration of the shock state, as patients dying early in shock do not show it. The diagnostic feature, clinically speaking, is that of hemoconcentration. This state is found in all cases except where the shock state is secondary to hemorrhage and then one finds hemodilution.

An important concept is, as Moon[13] points out, the liability of a vicious circle. This applies to those cases in which the systolic blood pressure has been hovering around 70 to 80 for a matter of hours. The danger in these cases is that tissue anoxia once having set in will lead to acidosis and defective metabolism, with resultant capillary atony and then a consequent reduction in blood flow and thus greater anoxia.

Nowadays we are all aware of shock, but that there is a condition which we might call a state of chronic shock or what Moon calls sub-lethal shock[14] we are inclined to ignore. Here due to malnutrition, wasting illnesses, and prolonged recumbency, a pathological state develops which is akin to shock, and as Moon shows predisposes a terminal bronchopneumonia. These cases then would naturally be poor operative risks, and any medication or anesthetic known to aggravate shock would be contraindicated. Such a condition we have in Case XIII.

6. *Air Embolism.* Experimental work by Joannides and Tsoulos[15] is interesting in this regard. They found that the speed of air embolism is as important as the amount of air. They injected 200 cc. of air into the femoral vein of dogs and found that it was a fatal amount when given in less than five minutes. However, if this same amount of air was given in thirty minutes or over it was not fatal. This would be an argument in favor of slow dissection especially when operating in a region where veins are known to have a negative pressure, such as the chest and neck. However, the important fact in the consideration of these two cases is, as mentioned above, that only relatively small amounts of air need be injected into the pulmonary veins in order to cause death. This is because air sucked into the pulmonary circuit is immediately pushed into the cerebral arteries along with the rest of the systemic circulation.

The mechanism of death in these cases is due either to (1) asphyxia and anoxemia, as the heart and arteries are filled with froth, and energy is expended in mere churning, or (2) central anemia because of obstruction in the cerebral vessels due to air bubbles. Anoxemia results, followed by a constrictor paralysis which is in turn followed by dilatation of the vessels and subsequent diapedesis of red blood cells. This explains the petechial hemorrhages so commonly present in these cases.

7. *Anesthesia.* In general we might say that anesthesia has had to take the blame for a greater number of operating room fatalities than in our opinion has been warranted. It is far too easy to dismiss a case as an anesthetic death without due consideration of the many physiological factors entering into the picture. However, it is true that anesthetic deaths are all too common and could perhaps be diminished in number by proper preoperative care, wise choice of the anesthetic agent, and consideration of the various secondary factors which might make the patient a definite risk.

Gwathmey[16] found by reviewing the records in the Chief Medical Examiner's Office in New York City that from 1928 to 1932 there were 219 deaths, or forty-four per year. These were considered to be true anesthetic deaths, to which no pathological condition of the patient could be found to have contributed. He stressed the importance of proper preliminary medication in the prevention of anesthetic deaths with the consideration of psychic as well as organic factors. In this paper we do not

intend to go into the physiology of anesthesia. However, it is perhaps expedient to mention a few pitfalls that have been brought to our attention by a study of our own cases:

Local Anesthesia. This we will dismiss with little more than mentioning an important experimental observation by Beecher[17] that while 40 mg. per kg. of novocaine when injected rapidly intravenously will kill a cat, when injected slowly 400 mg. per kg. may have no harmful effect at all. That there are cases on record of sensitivity to novocaine is well known. This has been one of the suggested reasons for the so-called "pleural shock." However, we do not believe that this had any bearing on our own series of cases.

General Anesthesia. As for general inhalation anesthesia, there is a long list of available agents, and they have many different indications and contraindications. Some agents, such as chloroform, have been largely condemned except under certain rare circumstances. Beecher[17] states that there is absolutely no margin of safety in chloroform anesthesia; 20 to 40 mg. per cent will seriously impair heart action, and yet 18 to 40 mg. per cent is necessary for full narcosis. The mechanism of death is considered to be cardiac. The drug is known to be toxic on the heart long before it is on the respiratory mechanism.

Ether Anesthesia. Ether convulsions are phenomena about which nothing positive is known. Many theories have been advanced concerning their etiology. Dodd[18] believes that atropine is partly responsible; Rosenow and Tovell[19] thought it might be a neurotoxin liberated from streptococci. Low serum calcium has been held responsible in some instances. Quite likely, however, many more factors are responsible. These cases almost invariably occur in the heat of the summer and they usually show evidence of toxemia.

Spinal Anesthesia. As stated before, fatal accidents due to spinal anesthesia probably occur secondarily to paralysis of the phrenic mechanism, the intercostals or of the respiratory center.

SUMMARY

1. Twenty-three consecutive cases of sudden operative deaths in which autopsies were performed occurring during a ten-year period in the Royal Victoria Hospital have been reviewed from both the clinical and the pathological points of view.

2. The purpose of this survey was to throw some light on the mechanisms concerned in such deaths, thereby enabling us to give more care to the preoperative and operative management of the different cases.

3. We believe that by applying Barcroft's classification of the different types of anoxia to the majority of these cases, it enables us to understand more readily the various mechanisms involved.

4. Other factors of importance in the causation of operating room fatalities as determined from our cases include aortic stenosis, cardiac decompensation, asphyxia, shock, so-called "pleural shock," hemorrhage, status lymphaticus, air embolism and anesthetic agents.

5. Finally, because of the various causes of death, the various precipitating factors involved, and the many different physiological mechanisms at work in these cases, it is apparent that to obtain the greatest degree of safety each poor risk patient must be treated individually by both surgeon and anesthetist and through consultation a definite plan of action decided upon.

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DIAGNOSIS AND TREATMENT OF ACRAL GANGRENE*

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AT first thought, one might suppose that the diagnosis and treatment of gangrene of the extremities is not a very involved subject. The diagnosis of gangrene is usually self-evident, and the treatment must, ultimately, be amputation in some degree or other. But a little thought will reveal that the subject is far from being a simple one. Gangrene is the dramatic terminal picture of deficient circulation but is not, in itself, an acceptable diagnosis. Instances of acral gangrene differ as to etiology and pathology and there is a concomitant difference in the treatment and prognosis. Two cases, for example, may appear quite similar on superficial examination and yet one may successfully be treated by an auto-amputation, or at worst a very minor local amputation while the other may require a radical high amputation for its correct management. Not only will a proper and complete diagnostic study in cases of gangrene of the extremities permit of intelligent and correct therapy, but more important, a full knowledge of the causes and types of gangrene is more likely to make the clinician "gangrene conscious" so that whenever possible he can forestall its development by the earlier diagnosis of certain predisposing vascular disorders.

CLASSIFICATION

Acral gangrene may be divided into two large clinical groups: The first group includes cases of gangrene developing in a limb without previous significant arterial disease, the first inkling of a pathological condition being the development of impending gangrene. The second group includes those cases in which there has been pre-existent arterial disease and in which *it should have been possible to foresee the eventuality of gangrene*. The responsibility of the physician, prophylactically speaking, is considerably greater in this latter group

GANGRENE DEVELOPING IN A LIMB WITHOUT PREVIOUS SIGNIFICANT PERIPHERAL VASCULAR DISEASE

Here we find those cases in which gangrene develops or threatens because of (a) trauma to a main arterial trunk, (b) thermal factors, (c) embolism, (d) chemicals or drugs, (e) thrombosis associated with postural stasis or systemic disease and (f) local infections.

It is not surprising that in this group, without pre-existing significant vascular disease, gangrene is never given a thought until there dramatically develops a cold, pulseless extremity associated with such other characteristic signs as a mottled appearance, anesthesia or parasthesia, loss of function and perhaps pain. Yet even in this group of cases a certain number could be prevented by the avoidance or protection against certain factors which are known to predispose to the development of such gangrene.

(a) *Trauma to a Main Arterial Trunk.* This is, perhaps, the least preventable of all forms of gangrene. There are various types of injuries to main vessels, any of which may produce varying degrees of gangrene distal to the injury. Such injuries vary from severance of the trunk necessitating ligation, to internal hemorrhage producing an aneurysm (false) which, by pressure, obliterates the main trunk. Whether or not gangrene develops after such an injury obviously depends upon whether or not sufficient collateralization can develop.

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This, in turn, depends upon two factors: (1) the overcoming of vasospasm in collateral vessels (vasospasm being invariably associated with such trauma) and (2) the collateral-forming potentialities of the region concerned.

FIG. 1. *Vasospastic gangrene:* Following an injury to the right subclavian artery, the right upper extremity became pulseless and cold, gangrene and ischemic contractures resulting as pictured. The artery was not severed, simply injured, because within a comparatively short time excellent and apparently normal circulation returned to the extremity. The gangrene and other damage evidently was the result of intense traumatic vasospasm. This could probably have been prevented by immediate regional sympathetic block. Such a chemical section should be empirically done in all cases of trauma to the big vessels, to counteract the invariably associated vasospasm.

Thus it has been shown[80,86,107,130] that if an artery is wounded there invariably develops a varying amount of vasospasm in the other vessels of the extremity; and Heidrich (quoted by deTakats[35]) showed that the percentage of gangrene after arterial ligation varied from 100 per cent after aortic or common iliac ligation to 0 per cent after ligation of the radial, ulnar or posterior tibial arteries, with a 37.2 per cent likelihood of gangrene following ligation of the popliteal as compared to 21.8 per cent following ligation of the common femoral. The "collateral-forming" potentialities ("blutegefühl") depend not only on the vessel or region involved but also upon the condition of the vessels. Trauma to a vessel in an extremity in which there is already a vascular pathological condition is obviously more serious than if the vessels be normal.

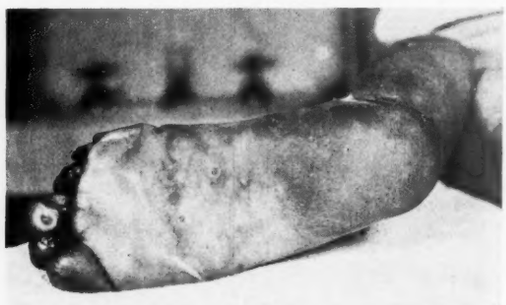

FIG. 2. *Gangrene from frost-bite:* The essential pathological status of such gangrene is an initial vasospasm with secondary thrombosis. Such gangrene is entirely preventable by proper protection from undue exposure. The initial treatment is counteraction of the underlying vasospasm. Débridement of the localized gangrene can be safely done, as it can be done in most cases of gangrene which develops in a limb without previous vascular disorders.

The fact that gangrene can result primarily from venous disorders rather than arterial disorders is frequently overlooked. It has been pointed out that venous thrombosis due to trauma or phlebitis can produce a reflex vasospasm of the arteries[14,34,35,85,113] which may, at times, cause sufficient arterial obstruction to threaten or actually produce gangrene. Moreover, varicose ulcers, the result of simple varicosities or varicosities associated with arteriovenous fistulas, are really localized areas of superficial gangrene from marked venostasis.[5] A too tightly applied cast may cause vascular disturbances principally through its interference with venous circulation.

The treatment of gangrene that results from the traumatic stoppage of blood through the main arterial trunk is aimed primarily at its prevention while it is still impending and before it becomes inevitable. Such treatment seeks the maintenance of effective nutrition until collateralization fully develops. This is accomplished by (1) overcoming vasospasm and (2) vein ligation. Leriche[86] has emphasized the rôle of vasospasm in trauma to, or ligation of,

arterial trunks and has pointed out that if it is necessary to ligate an artery, a segment should be removed between ligatures, this

Fig. 3. *Gangrene from embolism:* Such gangrene can be minimal as here illustrated, or quite extensive. In the extensive forms vasospasm should be actively combated. Successful embolectomies have been done, but there is some reason to believe that such a procedure can be equalled in results by release of vasospasm. It is sometimes difficult to differentiate thrombosis and embolism, but the treatment in both types of gangrene is essentially the same. The resulting gangrene can be treated by a localized amputation or débridement and good healing of the stump can be anticipated.

seeming to lessen the degree of vasospasm. Other methods he has recommended for combating vasospasm include peri-arterial sympathectomy above the lesion, anesthetic infiltration of the adventitia and chemical or surgical section of the sympathetic flow. Gage and Ochsner[59] have employed sympathetic block in ten cases preliminary to ligation of a main arterial channel and in none did gangrene ensue. Papaverine hydrochloride is likewise useful in overcoming vasospasm.[36,118]

Oppel[116] first suggested the ligation of a vein, the popliteal, in preventing gangrene in which the arterial circulation was deficient, the theory being that this produced a more effective tissue pressure of the available nutritive material by preventing its too rapid removal via the intact venous system. Holman and Edwards[69] showed experimentally that if the vein is ligated higher than the artery, both the blood pressure and the blood flow is increased in the distal stump of the ligated artery. This procedure has been used by a number of clinicians in treating gangrene which is the result of vascular disorders[12,37,87] as well as of trauma. It has

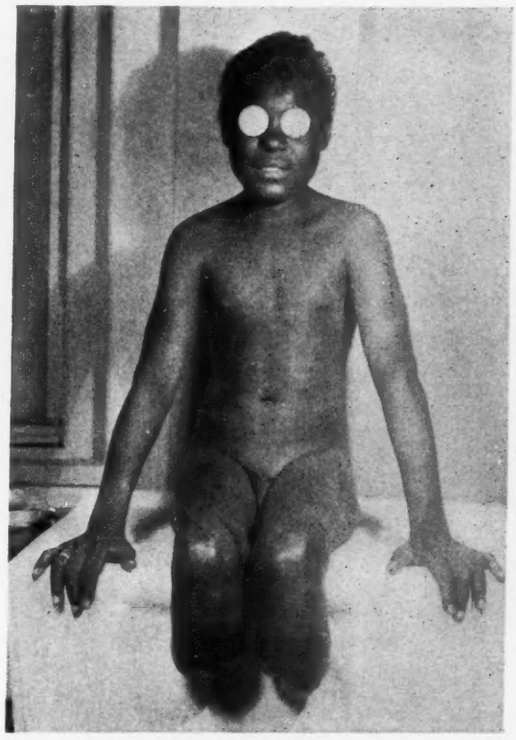

Fig. 4. *Bilateral "juvenile" gangrene:* So-called "juvenile" gangrene is not a clinical entity but results from a variety of causes. In this case, the cause was bilateral thrombosis occurring in the course of a systemic infection (typhoid). Amputation was confined to the area of demarcation with good healing of the stumps.

been recommended that whenever it is necessary to ligate a main artery, its satellite vein should likewise be ligated, thus lessening the likelihood of gangrene developing. The value of this procedure, in selected cases, has been shown by the clinical and experimental observations of Brooks and his associates.[22,23,24] However, Leriche[83] has recently pointed out that he believed the value derived from vein ligation is the result of relaxation of vasospasm and he has abandoned the procedure for more direct methods of relaxing vasospasm.

We have seen no results whatsoever in the use of suction-pressure treatment in the development of collaterals in cases of traumatic interruption of a main arterial channel; perhaps this is because the benefits

from this form of treatment are evidenced too slowly to be of practical value.

In summary, then, the treatment of gangrene or impending gangrene following injury to a main arterial trunk is principally the relaxation of vasospasm by novocain block of the regional sympathetics and the use of papaverine. If a main arterial trunk is ligated, its satellite vein is likewise best ligated. Once actual gangrene develops, it can be allowed to proceed to auto-amputation or when well demarcated, a local removal of the dead tissue may be done.

Two additional procedures frequently used are the conservation of the heat of the extremity by wrapping it in sheet cotton or some similar material, and the maintenance of the extremity at a level slightly below that of the heart. The use of the uncontrolled heat (light) cradle and the elevation of the extremity, procedures which are frequently used, cannot be condemned too strongly. This applies to gangrene of any origin (with the possible exception of infectious gangrene, v.i.). As Freeman[57] has pointed out, gangrene results from a discrepancy between the demands of the tissues and the supply of blood to meet these demands. Furthermore, the metabolism of tissue increases directly with its temperature. If a heat cradle is used, it should be carefully regulated to body temperatures.[133,143] If the heat be excessive, the development of gangrene is more likely to be facilitated than prevented. It is usually sufficient to insulate the extremity against loss of heat. As Leriche[86] has pointed out, external heat is of little value as it is not the skin but the deeper structures that need blood and this can be little influenced by external heat. Elevating the leg serves to hasten venous drainage from the part and this is more likely to result in gangrene than if semistagnation is encouraged by keeping the extremity a little below the level of the heart.

(*b*) *Thermal Gangrene.* As pointed out above, heat, under certain circumstances, may encourage the development of gangrene. But it is cold that most typically produces such a lesion, the so-called "frost-bite." Even in the deep South this lesion is occasionally observed.

Theis[147] has pointed out that the pathophysiology of frost-bite is primarily cutaneous vasoconstriction resulting in a short-circuiting of arterial blood directly into the veins. Thus the superficial structures are not irrigated with blood. He divided the lesions into three stages: (1) acute vasomotor ischemia in which the injudicious use of heat may be distinctly harmful because of increasing demands on tissues incapable of meeting them due to the vasoconstriction. If thrombosis does not occur, complete recovery may ensue. (2) Chronic frost-bite or chilblains may follow the acute stage. (3) Necrosis and gangrene may occur if the vasoconstriction is unrelieved and thrombosis occurs.

Brahdy[19a,20] has made some interesting observations on frost-bite among New York City employees. He found that a temperature below 14°F. constitutes an industrial hazard, particularly if the individual has diabetes or arteriosclerosis. The important prognostic point, he found, was the length of exposure after the first symptom. Brahdy has emphasized that the only satisfactory preventative against frost-bite, if cold exposure must occur, is in the use of adequate clothing. We have seen no real benefits from suction-pressure treatment in the few cases that have come under our observation, nor has Brahdy. Murphy,[108] however, has reported good results. If gangrene threatens, the best treatment is the protection of the part against further heat loss and the combating of vasospasm by papaverine or regional sympathetic anesthesia. Once definite gangrene is present it may be allowed to proceed to auto-amputation or a strictly local amputation may be done.

(*c*) *Peripheral Embolism.* Arterial embolus is of particular interest because it is one of the few acute vascular lesions amenable to radical and at times dramatic surgical intervention. Especially is this true

since the availability of heparin. Yet, because of the intense vasospasm present, sometimes equally dramatic results may be obtained from conservative measures directed at relaxing this vasospasm. The principal difficulty, if one contemplates surgery, is the differentiation of embolism and thrombosis.

Fig. 5. *Gangrene from thrombosis of the left radial and ulnar arteries:* Despite suction-pressure treatment the gangrene progressed until amputation had to be done above the wrist. The etiology was a thrombus, as proved at operation, apparently resulting from stasis from sleeping on this arm, an unusual development. The extension of the gangrene could possibly have been prevented by regional sympathetic block or by heparinization.

Embolism usually occurs suddenly with no previous significant peripheral vascular lesion. Usually the process is initiated with sudden severe pain, although this is not invariably present.[95] The clinical findings will obviously vary, depending on the number and location of the emboli; simple superficial areas of gangrene may be present or there may be massive gangrene of an extremity. This is preceded by a pale, pulseless extremity with anesthesia or parasthesia. According to the findings of McKechnie and Allen,[95] 50 per cent of embolic cases progress to actual gangrene. In 70 per cent of cases the embolus originates in a heart lesion,[76] while it occurs postoperatively in about 14 per cent.[39]

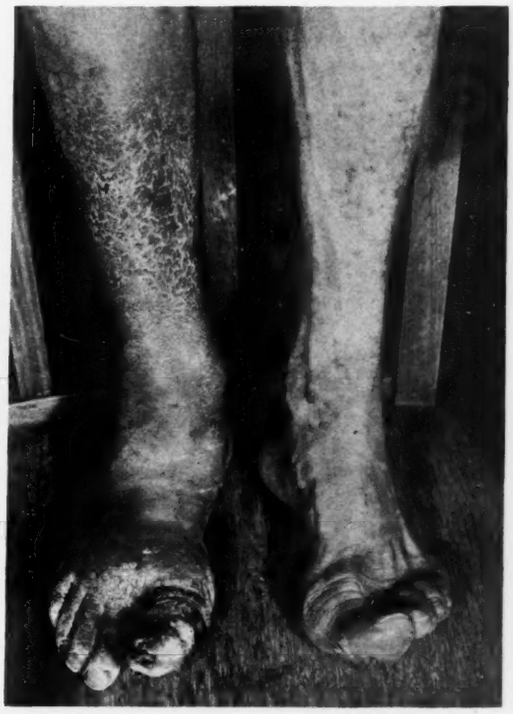

Fig. 6. *Infectious gangrene:* Particularly in diabetics is it important to determine if the gangrene is primarily due to vascular occlusion with secondary infection or if it is due primarily to a local infection with secondary thrombosis. In cases in which the underlying etiology of the gangrene is infection and thrombosis, local conservative treatment of the infection is in order, with a local amputation of the demarcated area.

According to Pearse, quoted by de-Takats,[45] peripheral embolism is more frequent in the common femoral (39.1 per cent) less frequent in the common iliac (14.92 per cent) and brachial (11.93 per cent) and least common in the ulnar (0.33 per cent). Koucky and his associates,[76] at Cook County Hospital, found that the lower extremity was involved in twenty of twenty-five cases. They consider the treatment of peripheral embolism under four types: (1) nonoperative, (2) arteriotomic operations, (3) arteriectomic operations and (4) amputative operations.

It is in the treatment of embolism that papaverine has found its greatest usefulness. Pal,[118] in 1914, first recommended the

use of papaverine to relax smooth muscle. Denk,[36] in 1934, introduced its use to combat vasospasm associated with acute embolism, reporting its use in ten cases. Approximately 50 per cent of cases with embolism failed to develop any gangrene. DeTakats has reported even better results.[43] Papaverine hydrochloride is best administered intravenously in ¼ to ½ gr. doses, every four to six hours. According to Burnett,[28] embolectomy should be done if definite circulatory improvement has not been noted in two hours. Embolectomy is probably useless after twelve hours, although recovery has been reported after forty-eight hours.[74] Gage and Ochsner[59] have reported four cases of femoral embolism in which the patients were successfully treated by novocain block.

Successful embolectomies have been reported by Linton,[91] Lund,[92] Pearse,[119] Key[74] and others. The use of heparin to increase the clotting time has been of definite value in preventing the occurrence of thrombosis at the site of embolectomy. Leriche[84] has recommended arteriectomy, as removing a segment of artery decreases vasospasm in other vessels of the extremity. But vasospasm can usually be overcome by papaverine or novocain block of the sympathetics.

One difficulty in contemplating an embolectomy is in localizing the site of the embolus, for the superficial signs are usually some distance removed from the obstruction. This can be accomplished by palpation of the pulses or better still by oscillometry or arteriography.[151]

If gangrene actually develops, it may be allowed to demarcate well before amputation unless the embolus be infected, in which instance the gangrenous area may become infected. In this case, amputation above the level of infection is frequently indicated, if localization does not rapidly occur.

In summary, the treatment of peripheral arterial embolism is first to combat the associated vasospasm which produces many of the clinical signs. This is best done by papaverine and/or novocain block of the regional sympathetics. If no improvement is noted in a few hours, and if the site of the embolus can be localized, embolectomy with heparinization (local or general) should be done. If gangrene develops despite these measures, a strictly local amputation can be done unless spreading infection develops.

(*d*) *Drugs and Chemicals.* Several different drugs and chemicals have, from time to time, been reported as producing gangrene. These include such drugs as carbolic acid, aluminum acetate, lead, carbon monoxide and copper sulfate. But the one of most importance clinically is ergot because of its widespread use.

A number of cases of gangrene have been reported after the use of certain ergot preparations, particularly ergotamine tartrate.[64,123,159] Yater and Cahill[159] point out that the ergot may produce occlusion of medium-sized and small arteries and arterioles due to severe vasoconstriction and resulting in thrombosis. Hyaline degeneration of the vessels follows the intense vasoconstriction.

McGrath[93] experimentally produced gangrene in albino rats with ergot and compared the pathological lesion with that found in thrombo-angiitis obliterans.

Ergot should be used cautiously and while it is being used the possibility of vascular lesions should be borne in mind, and its use stopped at the first sign or symptom suggestive of vasospasm. Actively, the vasospasm may be combated with papaverine or novocain block of the regional sympathetics. If gangrene actually develops, it can be treated by local débridement of the devitalized area.

(*e*) *Thrombosis.* Thrombosis is usually the determining factor in the production of gangrene from any cause. But apparently a thrombus can develop in an artery free from a previous pathological condition due to simple stasis, particularly in old people, and in the course of various infectious diseases in which apparently a local acute arteritis may precipitate the thrombus. Gangrene due to thrombosis has been reported in a variety of infectious diseases

such as scarlet fever, pneumonia, diphtheria, measles and chickenpox.[21,30,103]

Included in this group of cases of gangrene due to thrombosis might be that group of so-called "juvenile" gangrene, although Martin and Shore[104] have reported four cases and reviewed the literature, pointing out that gangrene in children, even when symmetrical, is not a clinical entity. Some may be due to embolism, some to endarteritis and some to autochthonous thrombi. Nearly all reported cases have occurred in the terminal stages or subsequent to generalized infections. Gangrene has even been reported in the newborn.[50]

The treatment in cases of thrombosis is, in the main, like the treatment of embolism, a condition which should be differentiated mainly because of the possibility of doing an embolectomy in the latter cases (v.s.).

(*f*) *Local Infections.* Sometimes, in the course of an infectious process in a toe, thrombosis occurs in the regional vessels and produces gangrene. Superficially, the gangrene may be indistinguishable from gangrene due to primary vascular disturbances. It is an important differentiation to make. As Williams and O'Kane[153] have emphasized, if the primary disorder is one of infection, with adequate deep circulation, the therapeutic indications

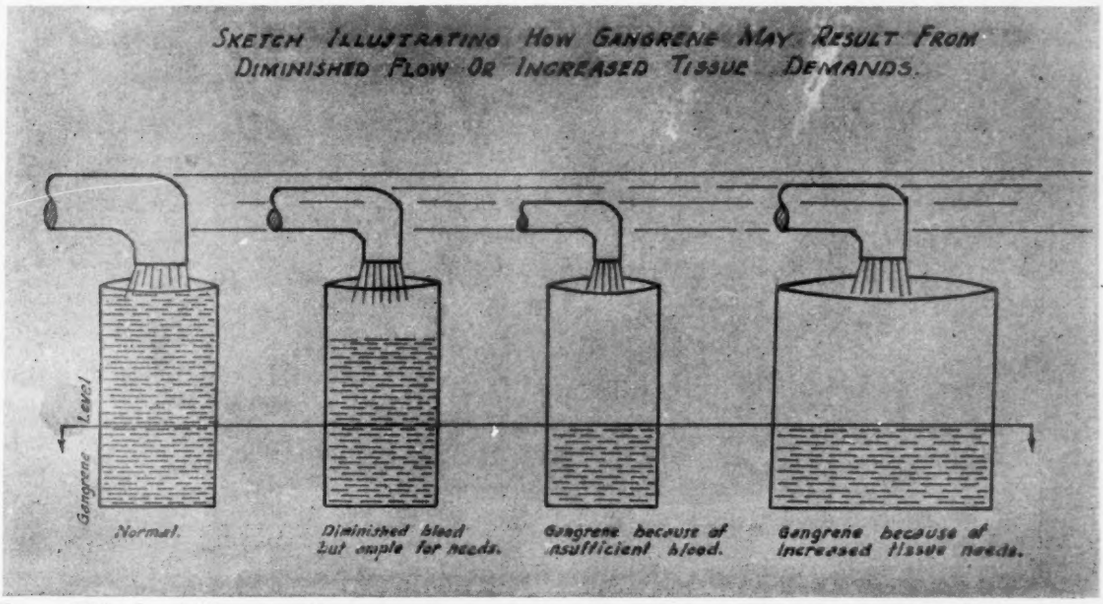
Sketch Illustrating How Gangrene May Result From Diminished Flow Or Increased Tissue Demands.
Gangrene Level
Normal.
Diminished blood but ample for needs.
Gangrene because of insufficient blood.
Gangrene because of increased tissue needs.

Fig. 7. This sketch illustrates how gangrene may be precipitated by a diminution of the blood flow or by a marked increase in tissue demands in a limb with already diminished blood supply. Such increased demands usually result from injury, excessive heat or cold, or infections.

are treatment of the infection and a strictly local amputation; if the infection is superimposed upon a primary vascular gangrene, considerably more radical procedures are indicated (v.i.). The differentiation is made by demonstrating the presence or absence of adequate circulation, principally by palpation of the pulses, oscillometry or arteriography. So-called "gas" gangrene is produced by mechanical blockage of the vessels by the large anthrax bacilli; the treatment is primarily toward the treatment of the septicemia, and any amputation done is to eradicate the source of infection.

This question of gangrene developing in an extremity free of previous significant vascular disorders may be briefly recapitulated as follows: In some instances, particularly in instances of trauma and in certain types of thrombosis and embolism, there is no way of preventing the vascular lesion, but the cautious use of ergot, the protection against excessive cold, the prevention of stasis in bedridden patients (if practical) are all prophylactic measures. If

gangrene impends, the prognosis is better than in limbs which are the seat of primary vascular disturbances because it is vasospasm, a remediable condition, that is productive of many of the symptoms. The principal therapeutic measures are (1) relief of vasospasm, (2) the use of the proper level of the extremity, (3) the conservation of the heat of the part, and (4) in embolism the carrying out of an embolectomy. If despite these measures gangrene develops, it usually can be allowed to proceed to well defined demarcation when a strictly local amputation will result in good healing.

GANGRENE DEVELOPING IN A LIMB WITH PREVIOUS SIGNIFICANT VASCULAR PATHOLOGY

The vascular lesions that may terminate in gangrene may be conveniently grouped into: (1) *infectious*, including principally (a) thrombo-angiitis, (b) thrombo-arteritis and (c) luetic arteritis; (2) *degenerative*, particularly arteriosclerosis, either senile or diabetic and (3) *neurogenic*, principally Raynaud's disease. With the exception of Raynaud's disease, the vast majority of significant lesions occur in the lower rather than the upper extremities.

In a consideration of this group of cases, it must be realized that the responsibility of the physician is quite great, for in the majority of instances if the vascular pathology be recognized and appropriate measures instituted, gangrene in most instances can be circumvented.

It is not our province here to discuss the diagnosis of peripheral vascular diseases. We would re-emphasize, however, that in the vast majority of individuals a correct diagnosis can be made by utilization of simple clinical methods and without the necessity of resorting to any special diagnostic procedures.[3,4] Clinical evidences of impaired circulation are: (1) intermittent claudication, (2) coldness of the extremity, (3) color changes (cyanosis, ischemia or rubor), (4) absent or deficient circulation as determined by palpation of the pulses and oscillometry, (5) trophic disturbances or (6) rest pain.

If one would simply routinely palpate the dorsalis pedis and posterior tibial, many cases of vascular disease would not be incorrectly treated for arthritis, fallen arches, neuritis or countless other foot ailments.[31] One should remember the observations of Reich,[125] however, regarding the pulses of the foot, otherwise palpation alone may be misleading. In 500 normal individuals observed clinically, the dorsalis pedis could not be palpated in 4 per cent, the posterior tibial was absent in 5 per cent. In another 8 per cent the dorsalis pedis was found misplaced. These findings were corroborated by anatomical studies.

The Prevention of Gangrene. As previously stated, it is not our purpose to discuss the differential diagnosis of the various types of peripheral vascular diseases, but rather the prevention and treatment of gangrene, which may result from such disease. Raynaud's disease has been considered in this group with previous vascular disease. It is realized that there is probably no primary pathological condition in the vascular tree but rather is there an overactive sympathetic system. But this disease gives symptoms months or years before gangrene develops so that if properly diagnosed gangrene can be prevented. If there is no response to conservative protective measures, sympathectomy may be resorted to with good results in many cases. Sclerodactylia is perhaps a more advanced form of Raynaud's disease in which extensive thrombosis and gangrene can occur. Sympathectomy, parathyroidectomy and other procedures have been of questionable value in checking its progress. Those cases with degenerative and infectious vascular disease may be considered as a group when we discuss the question of gangrene prevention.

Assuming that an organic vascular disturbance is known to be present, it is essential that the patient be made "foot conscious." The importance of the pro-

tection and care of the feet cannot be emphasized too often or impressed upon the patient too strongly. While this is especially so in the case of the diabetic patient, it applies to any patient with an organic obstructive vascular lesion. It is because of the insidiousness of the beginning of gangrene that it is so important to emphasize, to the patient, the potential dangers ahead. As John[71] has said, "If the beginning of gangrene were as noisily ushered in as an attack of biliary or renal colic, the results of treatment would be far different." The individual may actually have no symptoms, "their feet may be pulseless but still in a stage of compensation"[30] and then a precipitating factor causes additional strain on the available circulation, compensation breaks and gangrene threatens.

FIG. 8. *Thrombo-angiitis obliterans:* A, this shows beginning gangrene in a case of Buerger's disease. B, showing the healing that occurred after fifty-one hours of suction-pressure treatment. As a general rule, treatment is relatively conservative in thrombo-angiitis obliterans and one need not resort to amputation until ample conservative treatment has been found ineffective.

"The means for estimating peripheral vascular deficiency are almost as accurate as are the means of estimating the efficiency of the blood vessels of the heart and kidney. They are waiting to be put in general use by our profession. Once it

becomes the practice to study the peripheral vessels and advise people when there is a thin margin of safety in the blood supply of their legs, there are many things that can be done to avoid those critical periods of pain, infection, gangrene and amputation. Then, too, there will be a noticeable diminution in the number of patients treated for cramps, metatarsalgia, fallen arches and rheumatism." (Reid.[126])

The prevention of gangrene in an individual with peripheral vascular disease largely resolves itself into these two things: (1) the *intelligent* avoidance of precipitating factors and (2) the development of collaterals.

Avoidance of Precipitating Factors. There are three things which are particularly likely to cause a break in compensation by placing excessive demands on the available circulation and these are: (1) trauma, (2) infections and (3) thermal changes.

Trauma and Infections. These can best be considered together because they are so frequently associated clinically. Trauma may, in itself, by calling forth reparative processes endanger the effective vascularity of a limb, but its principal danger is in producing a lesion which is likely to become infected. In considering the question of trauma, one must think of minimal types which, in themselves, might be considered of little importance and yet in an extremity with deficient circulation may be all that is necessary to turn the tide adversely. The need of a properly fitting shoe, for example, cannot be overemphasized. A shoe too loose may rub sufficiently to produce blisters which are likely to become infected. A shoe too tight will further embarrass the deficient circulation. Patients must be cautioned against trimming corns and ingrowing toe nails as their feet, primarily because of deficient circulation, are more likely to become infected, and once infection develops, the added defensive demands may well strain the effective circulation to a point that "compensation" may break.

Veal and McFetridge[150] analyzed the precipitating causes of gangrene in 139 of 171 cases. Of these 139 cases, trauma was the precipitating factor in seventy-three cases. In the cases of Buerger's disease, the gangrene resulted from trauma in 28.5 per cent; in the case of arteriosclerotic gangrene, trauma was the cause in 47.2 per cent; in diabetic patients, the gangrene was precipitated by trauma in 68.2 per cent of instances. This indicates that particularly in diabetes is trauma likely to be dangerous; this is undoubtedly because of the increased susceptibility of diabetic patients to infections. Oard et al.[111] found in a series of forty patients with peripheral vascular disease that more than 50 per cent suffered injuries from ill advised treatment. Trauma, they point out, is the most frequent cause of open lesions in a limb with poor blood supply. Similarly, Barker[17] found that in 171 cases of gangrene associated with thrombo-angiitis obliterans, the gangrene followed therapeutic procedures in 35 per cent. In 115 cases of arteriosclerosis obliterans, gangrene followed therapeutic procedures in 39 per cent. Too often has the careless physician observed a red, painful toe and thoughtlessly incised it, thinking it to be an infection, only to realize that severe vascular disease was the cause of the red toe and that injudicious trauma might be the precipitating factor for the development of gangrene.

It is well appreciated that in diabetic arteriosclerosis one of the prime reasons for keeping the patient well stabilized with insulin and diet[1] is to lessen the likelihood of infection developing, because it is likely to precipitate gangrene if it develops in an extremity already the seat of circulatory embarrassment.

Thermal Changes. We have already pointed out that excessive heat as well as excessive cold, although operating by different mechanisms, may precipitate gangrene. Heat increases tissue demands, which if the vessels are not able to supply, may cause gangrene. Cold, by causing vasospasm, further embarrasses the circulation and may precipitate gangrene.

Development of Collateral Circulation. A consideration of the development of collateral circulation largely concerns itself with a consideration of the conservative treatment of occlusive peripheral vascular disease, for the aim of such treatment is increased vascularity in the involved extremity. Wright[156] has recently given an excellent summary of this conservative treatment. These therapeutic measures aimed at increasing collateralization may be enumerated as follows:

Fig. 9. *Thrombo-angiitis obliterans:* Although much cannot be said for the usefulness of the right stump, this picture illustrates the fact that healing in thrombo-angiitis obliterans can frequently be obtained after repeated localized amputations. As a rule, more conservative amputations can be done in thrombo-angiitis than in arteriosclerosis.

1. *Active Vascular Exercises.* Buerger,[27] a number of years ago, described the exercises which bear his name. In these exercises the lower limbs are successively raised, lowered and placed level, in an effort to increase vascularity mechanically. Allen[7] has slightly modified these exercises. It is difficult to evaluate the exact degree of improvement such exercises engender, but they have, clinically at least, appeared to be of value and are in widespread use.[72]

2. *Abstinence from Tobacco.* It has been repeatedly shown[16,77,101,136,158,109,110] that tobacco smoking has a definite vasoconstrictive action. Although some investigators have expressed the belief that it is the act of smoking rather than the actual tobacco that causes vasoconstriction, the fact remains that vasoconstriction results from smoking. While this factor is particularly operative in thrombo-angiitis obliterans, and while in severe occlusive disease the vessels may be able to respond relatively little to the vasoconstrictive impulses, it is obviously advisable in any type of organic vascular lesion, particularly Buerger's disease, to interdict the use of tobacco so as not to interfere with the development of collateralization.

Fig. 10. *Diabetic gangrene:* Although the area of gangrene was relatively small, the marked vascular impairment and the spreading infection necessitated an amputation above the knee as an emergency procedure.

3. *Use of Alcohol.* Wright et al.[156] have emphasized the fact that alcohol has a vasodilating effect. In severe occlusive disease, the vessels may be relatively little influenced by this drug; still it can be empirically used in the hope that a mini-

mum amount, at least, of vasodilatation may occur. The victims of occlusive vascular disease, particularly Buerger's, are

Fig. 11. *Arteriosclerotic gangrene:* This patient was treated conservatively until it was evident that no improvement in collateral circulation was developing. Amputation was then done at the lowest level commensurate with good healing, which in this case was determined to be above the knee. In the absence of infection or spreading gangrene, conservatism may be temporarily employed in arteriosclerotic gangrene and an elective amputation done when the patient and collateral circulation are in the best possible condition.

impressed with the necessity of "swapping alcohol for tobacco."

4. *Baths.* Various types of hydrotherapeutic measures have been recommended to "massage" the vessels by causing alternate vasoconstriction and vasodilatation, principally the "contrast" baths.

5. *Heat.* Locally, heat has been used to cause vasodilatation, but as has been emphasized already, care must be taken not to use excessive amounts of heat, thus increasing tissue metabolism beyond the available blood supply. Heat has likewise been used in an effort to cause vasodilatation reflexly. Thus Gibbon and Landis[61] have shown that immersion of the forearms in warm water will cause reflex dilatation of the vessels of the lower extremity. Wright recommends the use of the heat pad over the abdomen; deTakats used diathermy to cause dilatation of the vessels of the lower extremity.

6. *Typhoid Vaccine.* The use of typhoid vaccine to produce vasodilatation was first suggested by Goodman and Gottesman.[63] It has been recommended particularly by Brown,[25] Barker[15] and Wright.[156] Like most of the measures aimed at vasodilatation, this procedure is particularly effective in Buerger's disease because in this disease vasospasm is frequently more evident than in arteriosclerosis. Not being without danger, it is not recommended in the latter disease. Other measures which tend to cause vasodilatation and which are in themselves harmless, may be used even in arteriosclerosis for what value may be obtained.

7. *Hydremic or Plethoric Treatment.* The intravenous administration of saline, particularly hypertonic (5 per cent) and other solutions such as sodium citrate, have been used in order to increase blood viscosity and cause the blood to force its way into the vessels still patent, perhaps recanalizing some that are occluded. Koga[75] first introduced saline infusion for this purpose and it was introduced in this country by Meyer.[106] Silbert[134] introduced the use of 5 per cent saline and has reported excellent results[135,136] with its use, as has Samuels.[126] Saline has largely replaced sodium citrate recommended by Ginsburg[62] and Steel.[144]

8. *Vasodilating Drugs.* Various vasodilating drugs such as nitrites, theobromine, theocalcine, calcium, choline compounds, tissue extract and papaverine have been recommended to increase vasodilatation. While these drugs, particularly papaverine, are of value in acute occlusions, their use in chronic occlusions is not usually productive of marked improvement. While these drugs are of some value in thromboangiitis, they are of very questionable value in arteriosclerosis. But as they are largely harmless, they are frequently used for whatever benefit may accrue.

9. *Mechanical Therapy.* Various mechanical devices have been introduced for the purpose of supposedly developing

collaterals, or the recanalization of occluded vessels. The best known of these devises is the suction-pressure boot, reintroduced by Landis and Gibbon[78] and Herrmann and Reid.[67] Surprisingly good results have been reported by these authors, results which have not been confirmed by most observers. Our observations on the use of this therapy parallels the experience of deTakats.[41] We have used it in a variety of cases and we have found that it is efficacious in relieving rest pain and increasing claudication time in arteriosclerosis, even though no demonstrable changes could be observed by oscillometry or dermal thermometry. We have occasionally observed improvement in non-infected gangrene associated with Buerger's disease, but it has not generally seemed to decrease the area of demarcation. We have found it absolutely worthless in most cases of Buerger's disease and in acute vascular lesions, and its use in infected lesions has been found, as might be anticipated, to spread the infection.

The Sander's "vaso-oscillating bed"[129] has been recommended by Barker and Roth[18,19] and Wright.[156] It acts very similarly to the active exercises of Buerger and Allen, without necessitating any effort on the part of the patient. It is apparently of value in arteriosclerosis obliterans, but is of little value in thrombo-angiitis obliterans.

Reactive hyperemia and intermittent venous occlusion, as recommended by Collens and Wilensky[33] have produced varied clinical results.

10. *Neurosurgery.* In Raynaud's disease, the value of sympathectomy has been well established. Also in Buerger's disease, if it can be demonstrated that vasospasm is present to an appreciable degree, this procedure is likely to increase vascularity to a degree that gangrene may be averted.

As has been pointed out by Smithwick and White,[139] crushing or blocking the nerve supplying a painful toe may not only relieve the pain but it also may, by removing the vasoconstrictor influence, actually increase the available circulation and improve any local lesion present. Laskey and Silbert[80] have favored sectioning the nerve supply for the same reasons. Relief of pain is an important thing because it permits tolerance by the patient of various other therapeutic measures. Unrelieved pain is, in itself, sometimes the *raison d'etre* for an amputation.

In summarizing the prevention of gangrene in extremities with previous vascular disease, it might be said that the principal thing is to avoid trauma, infection or thermal changes which might increase the demands beyond the ability of the available blood supply to satisfy. Particularly in diabetic arteriosclerosis is it important to stabilize the patient and guard against infection. Various vasodilating procedures are of some value in thrombo-angiitis obliterans, as vasospasm is frequently associated, but in arteriosclerosis these procedures are of relatively little value because vasospasm is relatively slight. Various mechanical therapeutic measures give symptomatic relief, particularly in arteriosclerosis, but apparently do little toward producing any *demonstrable* increase in blood supply.

TREATMENT OF GANGRENE

Already the question of the treatment of gangrene occurring in limbs free from previous vascular pathology has been briefly discussed. There remains to be discussed gangrene occurring in limbs previously diseased, but we will confine ourselves to cases of thrombo-angiitis obliterans and arteriosclerosis (diabetic and senile) as these comprise the vast majority of cases.

1. *Thrombo-angiitic Gangrene.* In the discussion of gangrene which develops in a limb not previously the site of vascular disturbances, it has been pointed out that because the vessels, other than the one immediately involved, are essentially normal, the collateral forming ability ("blutegefühl") of the limb is excellent. Therefore, it is possible for the area of gangrene to be confined to a relatively small region and amputation anywhere above the demarca-

tion is usually attended with excellent healing. To a lesser degree, this same general idea applies to those cases of gangrene, or impending gangrene, complicating one of inflammatory vascular disease, particularly thrombo-angiitis obliterans. Here the factor of vasospasm frequently plays an important rôle; the vessels are capable of a remarkable amount of re-canalization. Therefore, when gangrene impends, energetic measures aimed at decreasing the vasospasm and increasing the effective circulation should be resorted to. These measures have been enumerated under the methods of conservative therapy (v.s.). But should gangrene actually supervene, frequently it is possible to do a limited amputation and expect healing to occur. Even if a more extensive amputation prove necessary, rarely need it extend above the knee.

As Reid has pointed out, it is no longer satisfactory to classify gangrene and determine the optimum level for amputation: it is necessary to know the actual degree of circulatory embarrassment and to evaluate the rôle of vasomotor nerves, mechanical obstruction, infection and the general condition of the patient. As Finney once said, anybody can amputate a leg, but it takes a good surgeon to save one. By an intelligent study of a case it is possible to do as conservative an amputation as may afford good healing, always bearing in mind the prosthetic necessities.

Allen and Meyerding[6] consider that thrombo-angiitic gangrene extending above the toes is always an indication for amputation, but that "cases of gangrene affecting only the toes in whole or in part should be treated medically provided pain can be relieved and economic conditions permit it." To quote them further: "Amputation of toes may be successful in two types of cases: those in which there is a sudden thrombosis of the vessels of the toes, and those in which either or both of the main pedal vessels pulsate normally, indicating that the vascular occlusion is distal to these areas."

Meleney and Miller[105] recommend, in gangrene associated with thrombo-angiitis, that amputation be below the knee if the popliteal artery is palpable, above the knee if it is not, although they admit that this criterion has not been entirely satisfactory. Perlow[121] recommends oscillometry and dermal thermometry after typhoid injections as means of determining the amount of vasospasm, thus getting an index of the best level of effective circulation, a guide to the best level for amputation.

Horton[70] has pointed out that in cases of thrombo-angiitis receiving little or no treatment, 60 per cent will require amputation within a period of ten years. Wright,[157] on the other hand, has shown that while the amputation rate was 70 per cent in former years, today this has been reduced to from 3 to 10 per cent in some clinics. Certainly with some of the newer therapeutic procedures a more conservative amputation can be done than was formerly thought possible. Amputation should really be considered a "last resort" in thrombo-angiitis. It should be contemplated only for (1) intractable pain, not relieved by conservative measures such as nerve section, (2) a spreading gangrene or one which will show no tendency to heal despite more conservative measures, and (3) infected gangrene which will not localize satisfactorily.

Confronted with a case, however, in which amputation is necessary, two things must be established: (1) the degree of vasospasm present and (2) the level of effective collateral circulation. The larger the element of vasospasm and the lower the level of effective collateral ability, the more conservative can be the procedure, provided the operation is commensurate with a good prosthetic application. Conversely, the less vasospasm present and the higher the demonstrable collateral forming ability of the limb, the higher must be the amputation. A discussion of the methods of determining the degree of vasospasm are beyond the province of this paper, but the methods of determining the level of effective collateral circulation are briefly discussed below.

2. *Arteriosclerotic Gangrene.* While diabetic (pre-senile) and senile arteriosclerosis are, pathologically, indistinguishable, clinically they present considerably different aspects. Thus arteriosclerosis occurs approximately ten years earlier in the diabetic patient; the operative mortality is nil in senile gangrene but is 3.6 per cent in diabetic gangrene;[52] amputation is more likely to occur and is of more serious import in the diabetic group; major amputations are more often done in the senile than in the diabetic cases.[55]

Despite these general differences, the treatment of arteriosclerotic gangrene is quite similar in the two groups, following certain definite lines, always bearing in mind that in the diabetic group there is a controllable factor which must be treated in addition to the gangrenous process. There are several points of differences between thrombo-angiitic and arteriosclerotic gangrene which should be constantly borne in mind. While not only is the five-year life expectancy following major amputation four times greater in patients with Buerger's disease than in those with arteriosclerosis, major amputations are necessary in far fewer cases of Buerger's disease than in arteriosclerosis.[55] Arteriosclerosis is less responsive to conservative measures because the tissues are older and less resistant to infection, many of the patients are handicapped with diabetes, renal or heart disease, usually larger vessels are blocked in arteriosclerosis and there is less degree of vasospasm present.[157] As a group, arteriosclerotic gangrene has a larger amputation mortality than does amputation in Buerger's disease.

In arteriosclerotic gangrene amputation must be done at some period, and usually it must be more or less radical. The deciding factor as to how quickly the amputation must be done is the question of infection. Obviously, infection is more serious in the diabetic patient because of his increased susceptibilities.

Conservatism is probably justified, as pointed out by Atlas[13] and deTakats[49] under the following circumstances: (a) gangrene localized to a single toe, (b) the gangrene well demarcated and showing no tendency to spread, (c) no constitutional evidences of toxic absorption, (d) no local evidences of cellulitis or lymphangitis, (e) no intractable pain and (f) response to conservative treatment. Such conservative treatment should consist principally of (a) complete bed rest, with the limb a little lower than the heart, (b) a protective cradle over the foot, *without bulbs*, but with the heat preserved in the part by wrappings, (c) some mild local antiseptic at the area of gangrene, (d) the adequate control of the diabetes if present, as well as general care of the patient and (e) the prophylactic injection of tetanus and gas bacillus antitoxin. Other measures such as vasodilating drugs and mechanical measures may be used, but are of questionable value.

The importance of the preoperative use of tetanus and gas bacillus antitoxin as a prophylactic measure is frequently overlooked. Eliason and his co-workers[53] reported, in 1937, some significant observations regarding the development of gangrene following clean wounds. According to them, Tanner, in 1923, had first reported gas gangrene following amputations through an allegedly clean field. From 1930 to 1937, fifty-two similar cases were reported. Sixty-one per cent of these cases occurred following amputations for diabetic gangrene. At the University of Pennsylvania and Philadelphia General Hospitals, in the period from 1930 to 1935, 6.7 per cent of major amputations (including traumatic cases) developed gas gangrene postoperatively, while Wilson, in Boston, reported an incidence of 2.6 per cent in a series of 420 amputations. In a small series of thirty-six consecutive amputations for either senile or diabetic arteriosclerotic gangrene studied at the Shreveport Charity Hospital, there was one case of gas gangrene developing postoperatively, an incidence of 2.8 per cent.

The mortality varies in this complication but is exceedingly high, particularly in that

following amputation for diabetic gangrene. The interesting fact to be remembered is that in the collected series, the general mortality from the complication of gas gangrene developing after an amputation was 73 per cent in those cases in which no antitoxin was used as compared to a mortality of 51 per cent in which it was used.

At the first sign of spreading gangrene or spreading infection (or if these are present from the start) amputation must be immediately carried out. Once it becomes necessary to amputate, two things must be determined: (1) the level to amputate and (2) the type of amputation to do.

Determining the Level at Which to Amputate. The type of amputation will obviously, depend to a certain degree on the level that the amputation can be safely done. It is, therefore, necessary to determine at what level circulation is apparently adequate enough to expect good healing. The old Heidenhain law to the effect that amputation is as a rule best done high as here one is assured of adequate circulation can not be blindly accepted; as while obviously it is true that the higher the amputation the more likely is the circulation to be good, still it has been repeatedly shown that the mortality increases progressively as the level of the amputation becomes higher. One is not justified in carrying out any procedure that carries a higher mortality than is necessary.

The old Moschcowitz test or Matas' modification is still an excellent one, even if frequently forgotten. In essence, the limb is rendered bloodless with an Esmarch bandage; after its removal the limb is watched for the point where the circulation returns rapidly, and this marks the level of effective circulation. The oscillometer and arteriogram are excellent devices to measure directly or visualize the level of efficient circulation. A newer test, and one which is widely used at present, is the histamine test. Eppinger,[54] and later Sir Thomas Lewis[88] showed that the intradermal injection of a small amount of histamine caused (1) a local dilatation of capillaries, venules and arterioles by direct action with production of a purple spot, (2) a reflex dilatation of surrounding arterioles with production of a *flare* and (3) increase in permeability of the smaller vessels, again by direct action of the histamine, with exudation of fluid into the tissues surrounding the site of injection and the production of a *wheal.* Starr[141,143] and deTakats[38] have adopted this procedure for studying the collateral circulation of an extremity. One-tenth cc. histamine phosphate is injected at several levels. Normally, the reaction to histamine is at its height in five minutes, there being a well developed flare and wheal. Deficient circulation is suggested by (1) delay in appearance of the reaction, (2) poorly developed flare or wheal and (3) failure of flare, wheal or both to appear. The wheal is of more significance than the flare.

There are a number of contradictory reports as to the value of this test. We have found it fairly reliable, although we have experienced difficulty in reading the test in Negroes. Perlow[122] has suggested taking the temperature of the flare in these patients as an index of the degree of reaction. The recent work of Friedlander and associates[125] places some doubt on the reliability of this test. They showed that skin and muscle temperatures and circulation were independent and that the fact that changes occurred in the skin did not mean that they occurred in the deeper structures. Undoubtedly, it is better to ascertain the level of effective circulation before operative procedures are begun. But it should not be forgotten that despite all these tests, if the area in which the operation is done is obviously avascular, the amputation should be done at a higher level.

Type of Amputation. Amputations are done chiefly for two reasons: (1) as an *emergency,* life-saving procedure in infection, sepsis, or spreading gangrene and (2) as an *elective* procedure to remove a painful or useless extremity. In general, the type of amputation done will depend on whether or not infection is present and secondly the

level at which the amputation can be safely done, based on a study of the available collaterals. The lower the level of amputation, the lower the mortality, but it must be remembered that rehabilitation will require a useful stump to which an effective prosthesis can be fitted. This not only requires a stump with a good, painless pad, but requires knowledge of the levels at which a successful prosthesis can be fitted. This question has recently been discussed in a series of articles in the *Journal of the American Medical Association.*[11]

Emergency Amputations in Septic Cases. Nearly one-half of the hospital deaths from amputations are due to necrosis or sepsis in the amputation stump.[146] Therefore, in most instances, the indications are clear for a circular amputation, usually without closure, at a level at which it can be expected to heal. Secondary amputations to get a good stump may be elected when the patient is in a better general state. This is the general method in which most surgeons handle the question of the septic case. Few follow Zierold's[160] teachings of more or less locally débriding the wound and doing the major amputation later, although in his hands he is able to get fairly good results. Veal[149] believes that the dangers from amputation lie in pulmonary embolism, and he has lately advocated ligation of the femoral vein at the time of amputation to prevent this complication. Experience is too limited to judge the value of this procedure at this time, but it may prove to be a distinct contribution.

In *elective* amputations one has a wider choice of procedures and is guided in his decision by (1) the level of effective circulation and (2) the prosthetic necessities. In summary, it should be remembered that the best sites for amputation, from a prosthetic standpoint are: through the toes, the upper middle third of the leg, the transcondylar region or the middle third of the thigh. Poor sites are through the tarsus or lower third of the leg and just below the knee.

If a localized amputation can be done through the toes or metatarsals, a good functional result may be obtained without the necessity of any artificial appliance. Of the higher amputations, the Gritti-Stokes has been the most popular, being a lower thigh amputation. Two amputations more recently devised and which are not as generally used or appreciated are the Beverly Smith amputation[137,138] through the leg and the Callander[29] transcondylar amputation. I have seen Dr. Smith demonstrate his amputation and it is a very clever one; it will frequently permit of safer amputation through a lower level than would otherwise be possible. Callander's operation is decidedly the one to do if a higher amputation is required; it carries about one-fourth the mortality of a circular thigh amputation and gives a most excellent functional result. As a general rule, amputations for arteriosclerotic gangrene can seldom be done lower than the mid-third of the leg and usually require amputation in the region of the knee.

SUMMARY AND CONCLUSIONS

1. It is important to classify accurately the type of acral gangrene present, as treatment and prognosis vary with the etiology and pathological status.

2. Acral gangrene occurs in two types of cases: (a) those in which there is no previous significant peripheral arterial disease and (b) those in which previous arterial disease has been present.

3. Grouped under those with no previous significant peripheral vascular disease are those due to (a) trauma, (b) thermal changes, (c) embolism, (d) chemicals and drugs, (e) certain forms of thrombosis and (f) local infections.

4. Grouped under those with previous significant peripheral vascular disease are those due to (a) inflammatory disease (e.g., thrombo-angiitis, thrombo-arteritis and syphilis), (b) degenerative disease (e.g., arteriosclerosis, both diabetic and senile) and (c) Raynaud's disease. The physician's responsibility is greater in this

group, for early diagnosis is important in the prevention of gangrene.

5. Certain prophylactic measures in the prevention of gangrene in those without previous significant peripheral vascular disease include protection from trauma, protection from cold, avoidance or careful use of ergot preparations and prevention of stasis in bedridden patients.

6. Active therapy in this group includes principally (a) relief of vasospasm, (b) vein ligation or embolectomy as indicated and (c) local amputations after demarcation.

7. In the prevention of gangrene in cases with peripheral vascular disease the principal thing is an early diagnosis of the disease.

8. If peripheral vascular disease is known to be present, prophylactic measures against gangrene are (a) development of collateral circulation and (b) the avoidance of precipitating factors.

9. Collateral circulation can be particularly developed in diseases with a large amount of vasospasm such as thrombo-angiitis. Collateral forming ability is minimal in arteriosclerosis.

10. Measures used to increase circulation in a limb with peripheral vascular disease include (a) relief of vasospasm by drugs, heat or sympathectomy, (b) hydremic or plethoric treatment, (c) active exercises and (d) mechanical measures including suction-pressure boot, oscillating bed and venous compression.

11. Precipitating factors are principally (a) trauma, (b) infection and (c) thermic changes.

12. In the actual treatment of gangrene one can usually be more conservative or limited in operation in thrombo-angiitis than in arteriosclerosis.

13. The level of amputation will depend on the amount of vasospasm and the level of effective collateral circulation. The more vasospasm and the lower the level of effective collaterals, the lower can be the amputation.

14. The type of amputation done will depend on (a) whether it is an emergency or elective procedure, (b) the level that amputation is considered most likely to afford healing of the stump and (c) the prosthetic possibilities of the individual case.

15. Two types of amputations are (a) emergency, usually in septic cases, in which the usual procedure is a circular method of amputation and (b) elective, in which the best amputations are (1) through the toes or distal ends of the metatarsals, (2) Smith's mid-leg, (3) Callander's transcondylar and (4) the Gritti-Stokes' supracondylar amputation. The Syme ankle amputation can at times be utilized if a good artificial appliance is obtainable.

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According to Bloodgood, infantile hypertrophy of the breasts is due to an ectasia of the ducts of the breast and to their distention with desquamated, degenerated epithelium. The etiology of this epithelial hyperactivity is unknown.

TRAUMATIC SURGERY

DISEASES OF THE GENITOURINARY TRACT

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INJURIES to the genitourinary tract, resulting from industrial accidents, are a very small percentage of the total numbers recorded each year. However, it is my belief that the Industrial Labor Commission has to pass on the merits of twice as many claims of injury to the genitourinary tract which are devoid of any descriptive incident or accident involving trauma. The most frequent entity, seen in this atraumatic group, is epididymitis. Many physicians erroneously label these cases as traumatic epididymo-orchitis in their reports, hoping thereby to facilitate the acceptance of the alleged claim. The claimant, many times, is the laboring type, who, through misinformation, associates scrotal swelling with the much used and abused term "strain." He is indignant when told that his swollen testicle is a complication or extension of his kidney, prostatic or urethral infection. Many patients examined for atraumatic epididymitis give the story of the alleged muscular effort taking place on Friday, with the appearance of swelling on Sunday and the subsequent report of the alleged strain being made on Monday. One wonders whether this swelling did not result from the Saturday night social activities. In all these cases a prostatovesiculitis can be demonstrated by smear and culture of the prostatic secretion.

In epididymitis it is important that the treatment not be restricted to local and general rest, plus ointments and hot and cold applications, but it is also necessary to ascertain the initial focus, culture the organism and institute proper chemotherapy in hopes of eradicating the offending organism. Epididymitis is known for its tendency to have acute exacerbations.

Because the external genitals are exposed they are the site of most of the injuries of the genitourinary tract. Injuries to the penis are many and bizarre. Claims of fractured penises have come before the Labor Tribunals. Since the organ has to be in the state of erection in order to be fractured, it is questionable whether industry should be responsible for such an accident. Contusions, hematomas and evulsions of the cutaneous areas are not uncommon and are handled by the usual surgical routine for such injuries.

Recently, a patient received an injury in which the terminal one-fourth inch of the glans penis, to the right of the meatus, was removed as the result of an accident. His subsequent recovery was rapid. However, the tip of the glans, on the uninjured left side, protruded beyond the meatus and was pulled to the opposite side, due to the cicatrix on the right side. This deviation to the right caused the following mechanical interference to the free flow of urine: When the man voided, the stream would strike this obstruction and change its direction to an acute right angle. He claimed disability because of this stream deflection. He refused to have an amputation of the distal one-fourth inch of the glans penis on the unaffected side. Clinically, he was not disabled and had no physical disfigurement visible to the public. Since there was no schedule loss for such an injury he was given a cash settlement to close out the nuisance value.

TREATMENT

Treatment of penile hematomas, etc., are the same as localized bleeding elsewhere. However, if the bleeding is within the corpora cavernosa the end result is fre-

quently an organized clot, resulting in total or partial priapism. Surgical evacuation of clots promptly relieves this condition.

Lacerations of the penile urethra should receive instant attention by splinting the urethra with an indwelling urethral catheter for forty-eight hours. The end result is always good, if following the accident, the catheter is inserted into the bladder before the patient has voided in order to prevent urinary extravasation by way of the tear. Should the patient have voided before the installation of the catheter, and a phlegmon develop in the penile shaft from the extravasation, the phlegmon should be incised and drained in the manner of a peri-urethral abscess. The prophylactic use of the sulfa drugs is indicated, while the patient wears the indwelling catheter, to prevent or limit a catheter urethritis and prostatitis.

Trauma directly to the scrotum can and does cause rupture of the testicle, hydrocele and hematocele. These are handled surgically. In addition, the hydrocele can be obliterated successfully by aspiration of the sac and introduction of sclerosing solution.

Torsion of the testicle is an entity which is too frequently missed by the first examining physician who records it by that familiar label "traumatic epididymitis" and treats it as an inflammatory lesion, with the result that the claimant has a long period of unnecessary, painful suffering, with the added loss of time from industry, plus the inevitable useless atrophied testicle. The clinical story is typical: (1) A messenger, riding a motorcycle, runs over a bump, causing him to lose his seat and he sustains immediate pain in the affected testicle, usually accompanied by nausea and vomiting. (2) A busboy, carrying a loaded tray, steps on some spilled food, causing him to slip. He makes a great effort to regain his balance and not drop the loaded tray. He succeeds only to have immediate and continuous pain in the affected testicle. Many more incidents of the same pattern could be cited in which the patients were erroneously treated for an inflammatory rather than a mechanical lesion. Exquisite tenderness, confined to the scrotum, which defies satisfactory palpation due to extreme pain, plus the typical history, should immediately suggest to the examining physician that he is dealing with an acute torsion, the care of which is surgical and not palliative.

Rupture of the urethra and bladder, either singly or in combination, is frequently seen as part and parcel of crushing injuries in and about the bony pelvis, and it is highly important that the presence of these injuries be determined early and proper measures be taken immediately to short-circuit the urinary outflow before the dreaded urinary extravasation is clinically evident. I make it a rule that all patients with pelvic injuries seen in consultation have an indwelling flexible catheter inserted for forty-eight hours. Failure in catheterization strongly indicates a break in the urethral continuity. If catheterization is successful, the question of ruptured bladder can not be accurately determined by the presence or absence of bladder urine. It is not advisable to introduce per catheter a known quantity of sterile fluid and then measure the return. If the return fluid equals the amount introduced, the deduction is that there is no rupture. However, if the rupture exists, the introduction of fluid causes either a spread in the existing peritonitis or space of Retzius' extravasation, depending upon whether the bladder rupture is intra- or extraperitoneal. The safest method is to introduce one or two ounces of air by means of a sterile syringe, compress the catheter, detach the syringe and place the end of the catheter into a basin filled with fluid, (the basin resting on the mattress, beneath the level of the bladder) and then release the catheter compression. If air bubbles into the fluid with force, the bladder is not ruptured.

There are two reasons for cystotomizing all patients with a ruptured urethra resulting from crushing injuries: First, the rupture is frequently an evulsion of the bladder neck beneath the suprapubic arch. If the

rupture is posterior to the membraneous urethra, the extravasation will point into the iliac gutters or space of Retzius and with the suprapubic approach this area will be adequately drained. Second, concomitant bladder rupture may exist which would not be detected from a perineal approach. In addition, secondary repair of a ruptured urethra, if necessary, can be done with greater dispatch if a preliminary cystotomy has been performed, thereby giving the operator a dry perineum.

Kidney injuries divide themselves into two large groups: (1) those cases which result in a perinephritic spill of blood, urine or both and (2) intrarenal injuries, such as subcapsular hematomas and intrapelvic lacerations with ensuing hematuria. The first group calls for surgical drainage at the earliest opportunity, and nephrectomy if necessary. In the second group, each case is a rule unto itself. Surgery in this group should be the last resort.

Ureteral injuries are a rare entity and are usually associated with perforating injuries to the abdomen. They are always overshadowed by the symptoms resulting from a concomitant ruptured intestinal viscera.

Back injuries are the most costly group from the standpoint of time and medical expense. Every ambulatory patient with an obscure back injury should have a prostatic smear and culture performed. Patients with injured backs requiring long periods of complete immobilization and having associated spinal column and cord injuries, often present an added complication, namely, the so-called orthopedic urinary calculi. The first question raised is whether the calculus antedated the accident or if it is the result of the osteoporosis incident to complete immobilization which causes the mobilization of calcium with attendant hypercalcemia. A decision could be reached more easily if the initial *x*-ray taken, following the accident, would include detailed films of the kidney areas as well as the spine, and also if frequent urine tests during the patient's inactivity were recorded. It is a common finding in cases of osteomyelitis of the pelvis and lower extremities that the plates taken cover only these areas, hence, the disputed question of cause and relation of the calculus. It is important that all injuries requiring long periods of inactivity have *x*-rays made of the kidney areas following such accidents to exclude further controversies.

Apropos of kidney calculi, too many cases of back strain are treated too long before the underlying renal pathological condition manifests itself by hematuria, passage of a calculus or by good medical inspection. The descent of stones from the kidney into the ureter, while at work, causes immediate disability. Does the work initiate the moving of the stone? Many times the Commission has ruled that the replacement cystoscopically of the stone from the ureter back to the kidney pelvis to terminate the pain disability, is all that is required of the employer to discharge his liability if it is proved that the worker was performing tasks that would precipitate the moving of a calculus.

All too frequently are cases recorded of hematuria alleged to be caused by some obscure accident, such as lifting a plank, etc., hours before the initial bloody micturition. Examination discloses the source of bleeding to be from advanced carcinoma of the bladder, an enlarged, engorged prostate or some renal pathological condition such as neoplasm, stone or tuberculosis. By the greatest stretch of the imagination one cannot state that the underlying condition is caused by this lift. Did the lift cause the bleeding? Again, who can say? Bloody micturition is not immediate and, furthermore, these underlying conditions bleed independent of outer body activity because of their progressive destructive nature. The Death Calendar frequently hears claims that have for their premise that death was caused by some trivial accident. The death certificate will give bladder carcinoma and uremia as a cause of death and strenuous attempts are made to prove the facts causally related.

The urological care of the paralyzed bladder resulting from spinal injuries is a very important part of the injured person's treatment. Immediately following the accident closed tidal drainage is the ideal method to be instituted in order to avoid overdistention of the bladder with its attending stasis and infection. This type of treatment is a complicated one and cystometric readings must be made and properly interpreted at frequent intervals so that the manometric pressure of the apparatus may be changed from 2 to 5 mm. of mercury for the atonic cord bladder up to 20 to 30 mm. of mercury for the hypertonic bladder. The important consideration in the care of bladders, whose nerve supply has been interfered with, is to set the organ at rest immediately by an indwelling catheter, and in so doing, use a soft catheter, a No. 14 to 16 French. The larger the catheter, the greater the chances for urethral and prostatic infection. Place the patient, as soon as possible, on a régime of sulfanamides by mouth, plus increased fluid intake. If only the bony portion of the spinal column is involved, this treatment will suffice until the shock and edema have subsided; then micturition will be restored gradually. If the cord is involved with permanent damage to the bladder nerve supply, tidal drainage is the best method to institute until a so-called cord bladder is established. This end result may be obtained only one to three years after the cord injury.

In industry, the claim of impotence avails naught since one does not have to be potent to make a living. In the state of New York there is no fixed schedule loss for the complete loss or functional derangement of the urological organs. A person losing a toe or finger is awarded a sum fixed by law, not so in the loss or damage to a kidney, testicle, etc. As a result, litigation is protracted.

The world is claim-minded and this applies to the medical profession as well as to the people of industry. Attempts of doctors, under oath, to rationalize that indirect trauma, such as the opening of a drawer of silk stockings, causes nephroptosis in a thin, long-waisted female, and that orchidectomy performed on a sixty-eight year old man, because of trauma, would six months later cause prostatic hypertrophy with ensuing retention, due to sudden endocrine inbalance as a result of the orchidectomy, is ludicrous, to say the least.

STONES IN THE DUCTUS CHOLEDOCHUS

AN ANALYSIS OF 2,602 CASES OF BILIARY TRACT DISEASE AT ST. VINCENT'S AND HARLEM HOSPITALS IN THEIR LAST 250,065 HOSPITAL ADMISSIONS

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DURING the last decade many changes and considerable progress have been made in the treatment of calculi of the extrahepatic system. This is due primarily to a more complete and better understanding of the problem, derived from experimental research, a finer appreciation of the biochemistry of the liver, and a painstaking analysis of the operative findings and follow-up results of many experienced clinicians and surgeons which has been aided and abetted by cholangiography. In many of the larger hospitals and clinics of the country, it has now become an established routine to investigate the common duct in most cases of cholecystitis, not by palpation alone, but by routine aspiration or by drainage and probing.

Although the criteria for opening the common duct varies with different surgeons, and the advisability of routinely dilating the sphincter of Oddi in cases in which calculi are found is not subscribed to by all, still the majority seem to be of the opinion that cholecystectomy alone will not give sufficiently satisfactory results in all cases, for the same reason that routine cholecystostomies of earlier years failed, namely, because there was left behind in the ducts either calculi, or infection, or both. More radical investigation and surgery than were usually attempted in the past is now believed to be essential and necessary.

The technic of the surgical procedures has been well espoused and illustrated in the literature of the last few years so I will touch only lightly upon it. However, in this article I am endeavoring first, to emphasize the recently recognized high incidence of stones in the common and hepatic ducts in cases which have been hospitalized and operated upon for acute or chronic cholecystitis or pancreatitis, and, secondly to clarify, as simply as possible, the indications as to what type of surgery should be attempted and when it should be undertaken. Thirdly, I present an analysis of 2,602 cases of biliary tract disease at St. Vincent's and Harlem Hospitals among their last quarter of a million hospital admissions from 1931 to 1941. Lastly, I present a case report of a patient in which a common duct stone or stones were not found at the time of operation, but which were subsequently passed spontaneously after the administration of certain medications which are advantageous in stimulating normal function of the biliary system.

No matter what the criteria of the surgeon may be, he always should be conscious of the danger, the possibility, and even the probability, of the existence of a stone in the common or hepatic bile ducts whenever an operation for gallbladder disease is attempted. To overlook such a stone may result in failure of relief from symptoms, or may even prove fatal.

INDICATIONS

The question of what indications should guide a surgeon in his judgment as to the advisability of routinely exploring the ducts in cases of cholelithiasis and cholecystitis differs in many minds. I will enumerate a few of their criteria:

Bettman and Tannebaum[4] reported that their experiences at Michael Reese Hospital have led them to believe that a common duct should never be opened unless it is

markedly dilated, a stone palpated or the icteric index has remained high at time of operation in a case with a previous history of jaundice.

Frank H. Lahey[19] has urged that at the time of operation for gallstones not only a cholecystectomy be performed but that the common and hepatic bile ducts be explored in all cases in which the common duct was dilated, the head of the pancreas thickened, the gallbladder thickened or contracted or a stone palpated, and when an aspirated common duct contains dark cloudy, or murky bile. Jaundice is not believed by him[18] to be a reliable sign of the existence of a common duct stone, for he found that jaundice was present in only 60 per cent of the cases in which he removed a common duct stone, while Judd[29] reports the existence of jaundice in only 73.4 per cent of his cases. Jaundice is usually a late sign that occurs after considerable liver damage has taken place.

It is the opinion of Graham[10] that if after restoring the biochemical balance there is undiminished pain, despite adequate sedation, or if the pulse rises, or remains persistently high, direct surgical attack is indicated, in cases of cholecystitis.

Beall[3] expressed himself to the effect that the great majority of the cases of stone in the common duct are not in need of emergency surgery, and he emphasizes the great preoperative value of fluids, sugar, intravenous calcium and transfusions.

Heyd and Hotz[13] emphasize that a pathological condition of common duct is usually secondary to that of gallbladder. They further urge that to prevent such a condition of the common duct early diagnosis and operation is necessary on the gallbladder. Lahey, Walters, and others agree with them on this subject.

Whipple[33] holds that in long standing chronic cholecystitis, acute obstruction and infection of the common duct, the duct should be opened and drained, for such obstruction may be due to a stone in the common duct or to a pancreatic lymphangitis. If an acute cholangitis is present with an acute cholecystitis, the indications for drainage of the common duct are more urgent than if just an acute cholecystitis were present. He asserts that acute attacks of gallbladder disease are often accelerated in the already diseased gallbladder by progressive common duct obstruction from calculi or neoplasms and by, or together with, the resultant circulatory changes in the walls of the diseased gallbladder. The attitude in the past of certain physicians that surgery should be resorted to only after jaundice and sepsis have failed to respond to internal medication is decried as erroneous. The axiom that it is unwise to perform extensive abdominal exploration in the presence of an acute or suppurative lesion within the peritoneal cavity is in need of modification when it is applied to surgery of the biliary tree. When one reviews a large series of cases and the literature on acute cholecystitis and observes how often, because of improper exploration, serious underlying disease in the common bile ducts is overlooked, this proverb becomes all the more improper, erroneous and outmoded.

Thus it may be said that in cases in which cholangitis exists, a stone is palpated, the common duct is dilated, murky bile is found upon aspiration or jaundice is present, it becomes urgent for the surgeon to open, probe and drain the common duct in any case of cholelithiasis and cholecystitis. To these indications, some would add those cases of chronic and acute pancreatitis because of the usual co-existing infection and the presence of calculi in the biliary ducts. Surgery in these cases should not be hasty nor should it be delayed, but rather attempted at the first opportune time when the patient's fluid and biochemical balance have been re-established.

INCIDENCE

The high percentage of stones in the common duct in cases of cholecystitis and pancreatitis is emphasized by many authors and surgeons during the past few years. Although the incidence of cholelithiasis as

found by all is fairly uniform, the percentage of stones found in the common duct varies greatly, and in proportion to the number of common ducts that are explored and drained routinely whenever any of the aforementioned indications are present.

Among the negro race, gallbladder disease is usually rare, this in spite of their dietary delights of fried foods and their frequently unbalanced or impoverished diets. However small the incidence of cholecystic disease, it is amazing to observe in young negresses, the occurrence of gallstones in a high percentage of the patients who are suffering from the hereditary condition of sickle cell anemia. At Harlem Hospital where between 70 and 80 per cent of the patients are of the negro race, only 604 of the 154,908 patients admitted in the past ten years were diagnosed as suffering from disease of the biliary tract, and the majority of these 600 were white people. The percentage of these cases at this hospital who had cholelithiasis was 35.3 per cent, and of these 5.9 per cent (twelve cases) had stones in the common duct, 6.8 per cent of the total operative cases had a choledochal calculus, while the common duct was explored surgically in only 8.5 per cent of the cases. In addition to obstruction of the duct by calculi, one patient was diagnosed as having his common duct obstructed by laboratory proved parasites of the Strongyloides stercoralis species. At Harlem Hospital less than four-tenths of 1 per cent of all hospital admissions were found to have complaints referable to their extrahepatic system, and the percentage for those of the negro race was even lower, about one-tenth of 1 per cent of all admissions. (Table 1.)

At St. Vincent's Hospital during the past decade, 95,157 patients were admitted and of these 1,998 were found to be suffering from disease of their biliary tracts. Thus about 2 per cent of the total admissions had irregularities of their extrahepatic systems. Of 1,971 cases of cholecystitis, 998 cases, or 51 per cent had biliary calculi and eighty-nine patients, or 4.6 per cent, had calculi in the hepatic or common ducts.

Table 1
Analysis of Incidence and Complications

	St. Vincent's Hospital	Harlem Hospital	Both Hospitals
Cases of acute cholecystitis (including empyema) (gangrene, suppurative)	449	260	709
Cases of chronic cholecystitis (including hydrops)	1,532	317	1,849
Total cases of cholecystititis	1,971	577	2,548
Total operative cases of cholecystitis	1,438	137	1,575
Cases of acute cholecystitis with cholelithiasis	243	73	316
Cases of chronic cholecystitis with cholelithiasis	758	130	888
Total cases of cholecystitis with cholelithiasis	1,001	203	1,204
Cases with calculi in ductus choledochus	83	12	95
Cases with calculi in ductus hepaticus	6	0	6
Total cases calculi in the extrahepatic ducts	89	12	101
Percentage of cases of cholelithiasis	51%	35.3%	47.2%
Percentage of cases of cholelithiasis with common duct stones	5.7%	6.8%	6.2%
Percentage of operative cases of cholelithiasis with common duct stones	5.3%	7.3%	5.5%
Percentage of common duct drainage	6.4%	8.5%	6.6%
Percentage of common duct drainage where stones were present	82.8%	86%	82.9%
Obstruction of common duct by parasites	0	1	1
Obstruction of common duct by stricture	3	0	3
Cases of cholangitis (acute)	45	7	52
Cases of pancreatitis	51	0	51
Cases of intestinal obstruction	2	0	2
Cases of cholecystoduodenal fistulas	2	0	2
Cases of external biliary fistulas	12	0	12
Cases of adenocarcinoma of gallbladder	0	4	4
Cases of stab wounds or perforation of gallbladder	0	3	3
Total cases of disease of extrahepatic system	1,998	604	2,602

Of those 998 cases of cholelithiasis, 9 per cent had common duct calculi. The common duct was explored surgically in 7.7 per cent of the 1,438 cases in which the patients were operated upon, and in these 5.7 per cent were found to have common duct stones.

troubled by embarrassing adhesions about the gallbladder. In addition there were fifty-two cases of cholangitis, only twenty-two of which apparently were not associated with calculi of the common duct or disease of the gallbladder. Seven patients had cholecystogastrostomies performed.

TABLE II

SHOWING COMPARATIVE STATISTICS OF OVER 9,272 CASES OF CHOLECYSTITIS. THE PERCENTAGE INCIDENCE OF COMMON DUCT STONES INCREASES WITH THE PERCENTAGE OF CASES THAT HAVE THE COMMON DUCT DRAINED

Hospital Series, Author and Reference	Operative Cases of Cholecystitis	Per Cent with Cholelithiasis	Per Cent Common Duct Drainage	Per Cent Common Duct Stones	Per Cent Calculi in Drained Ducts
St. Vincent's Hospital, New York (1930–1940)	1,438	51	6.4	5.3	82.8
Harlem Hospital, New York (1930–1940)	137	35.3	8.5	7.3	86
Combining St. Vincent's and Harlem Hospitals (1930–1940)	1,575	47.2	6.6	5.5	82.6
Post-graduate Hospital, New York,[12,13] Heyd and Hotz (1920–1937)	3,306	69	7.7	6.3	86
Vicksburg Hospital, Mississippi, Willard Parsons[22]	X	X	16	15	94
Lahey Clinic, Boston, Frank Lahey[17,18] (1910–1925)	619	X	15	8.4	54.2
Lahey Clinic, Boston Frank Lahey[17,18] (1925–1935)	1,158	X	37.5	16.8	44.7
Massachusetts General Hospital, Boston, Allen and Wallace[2] (1930–1935)	1,228	X	32	13	42
Massachusetts General Hospital, Boston, Allen and Wallace[2] (1935–1940)	860	X	44.2	20.7	46.8
Peter Bent Brigham Hospital, Boston, David Cheevers[8] (1913–1935)	426	44	37.9	16.7	44.3
P. L. Mirizzi, Argentina[21]	100	X	44.2	23	52
Post-Graduate Hospital, New York, Carter and Hotz[7] (1920–1937)	3,306	Pancreatitis cases 53	Acute 78 Chronic 66		

Combining the cases of the two hospitals we find that in ten years 250,065 patients were admitted. Of these 2,548 had cholecystitis and 1,204 of these had biliary calculi, that is, 47.2 per cent. There were 101 patients (4 per cent) with stones in their common or hepatic ducts, ninety-five being in the common duct and six in the hepatic ducts, and one case with obstruction caused by the Strongyloides stercoralis. Three patients had penetrating stab wounds of the gallbladder and four are reported as suffering from adenocarcinoma of the gallbladder. Twelve patients had external biliary fistulas after previous surgery and two were found to have spontaneous duodenal biliary fistulas. Ten were

Of the 101 stones found in the ducts of the extrahepatic system, one of the six hepatic duct stones and four of the ninety-five cases of common duct stones had the calculi discovered at autopsies. Of the remaining ninety-six cases, stones were removed at eighty-seven operations and the remaining nine cases had the presence of the stones in the common duct proved by *x*-rays and clinical signs, with the patient refusing surgery. Of a total of 1,855 cases of cholecystitis in which the patients were operated upon at Harlem and St. Vincent's Hospitals, common duct stones were found in 6.2 per cent and the ducts were drained in 7.7 per cent of the patients. (Table II.)

Recently, Lahey[19] has explored the ducts in over 40 per cent of his operative cases, and has found stones in the common or hepatic ducts in nearly 20 per cent of these cases. Stones were found in 323 of the 718 cases in which he opened the ducts and in spite of the additional surgery of common duct drainage by a "T" tube, his morbidity and mortality diminished. A somewhat similar high percentage of calculi in the ducts was found by P. L. Mirizzi of Argentina[21] who reported that in his last 100 operative gallbladder cases 23 per cent had common duct calculi and one of calculus in the hepatic duct. Cheever[8] found stones in the gallbladder in 44 per cent of the 426 cases of gallbladder disease operated upon by him. Allen and Wallace[2] found common duct stones in only 13 per cent of their 1,228 cases and they explored 32 per cent of them. Heyd and Hotz[13] reported exploring 7.7 per cent common ducts in a series of 3,306 cases of cholecystitis and finding stones in 6.3 per cent cases. This incidence is quite similar to ours.

In a series of cases of pancreatitis reported by Carter and Hotz[7] common duct stones were found to be present in 66 per cent of the cases that had biliary tract disease and chronic pancreatitis and in 78 per cent of those with acute pancreatitis. They further noted that in all their cases of either chronic or acute pancreatitis on whom biliary tract surgery was performed all but 6 per cent of their cases showed biliary tract disease.

Aside from the danger of a stone in the choledochus and the existence of a pancreatitis, another important reason for exploring and probing the common duct in cases of acute cholecystitis is the lurking danger of the possibility of carcinoma of the ducts or the head of the pancreas. Rothenberg and Aronson[28] report eight recent cases of patients who were operated upon for cholecystitis in whom within three days to twelve weeks later they manifested signs that were later verified by either biopsy or autopsy as carcinoma of either the ducts or the head of the pancreas. In no one of these cases did the surgeon realize the existence of malignancy because of the acuteness of the gallbladder inflammation and the fact that seven of the eight had pain similar to that of biliary colic. In two of the cases carcinoma was suspected preoperatively but not verified at operation.

TREATMENT

Before any surgery is attempted in these cases, it is important to fortify these patients with intravenous fluids that will re-establish their normal biochemical and electrolyte balance, and when possible vitamin K and bile salts should be administered in ample dosage.

When enumerating a few of the important steps in the surgical procedure to be followed when exploration of the common duct is decided upon, it might be stated that many advocate when possible to drain through the stump of the cystic duct after incising its distal wall and extending the incision about one-quarter of an inch along the common duct, and then further exploring with the probe and scooping out any stones or gravel. The exploration should be carried out proximally as well as distally, for often calcareous materials will be found in the common hepatic or hepatic ducts. Drainage with a catheter down to or extending through the sphincter of Oddi or drainage of the common duct with a "T" tube of Deaver are all procedures advocated by various surgeons. The duct should be sutured securely about the inserted drain. If the patient's condition is extremely critical at time of operation, it may be advisable to drain the common duct away from its anastomosis with the cystic duct and leave the gallbladder for removal at a subsequent operation, or else to drain the gallbladder in addition, if circumstances permit.

Beall[3] who differs with most of the expressed opinions on the subject of drainage, believes that the common duct after being explored should be sutured so as to prevent the deleterious effect on the body of the loss of bile, which is manifested by a

loss of calcium and poor fat digestion. His technic is to close the incision in the duct and then drain down to it.

Routine aspiration of the common duct with an aspirating syringe is advocated by Lahey[19] for all cases of cholecystitis in which there is any suspicion about the contents of the duct. If the aspirated bile is cloudy or murky and has lost its golden glow, he recommends that the common duct be incised and drained. Such bile usually is infected and the probability is that some infection is present in the walls of the ducts.

Slow dilatation of the papilla of Vater is not only a safe procedure, but advisable following common duct exploration according to the work of Allen and Wallace.[1] This dilatation does not predispose to ascending infection nor does it seem to be permanent, or cause any cicatricial constriction. Although their cases showed an increase in the percentage of pulmonary complications, other complications were fewer and the drainage time was shorter. At one time all postoperative biliary colic following cholecystectomy was attributed to spasm of the sphincter of Oddi; however, such postoperative biliary colic is now believed to be the result of stones and gravel in the common duct or pancreatitis with a resultant spasm of the sphincter.

The high incidence of stones in the ducts as found by surgeons during their more thorough investigations of recent years leads one to assume that postoperative colic is caused by retained calculi. It is the rare case in which abnormal function of the sphincter of Oddi occurs alone as biliary dyskinesia.

If after removal of stones from the common duct and its subsequent drainage a choledochogram is performed either routinely or for failure of the relief of pain, and another stone is demonstrated, Walters, Butsch and McGowan[5,20] recommend using the technic of Pribram[25] or Osterberg, of injecting ether, or ether diluted with alcohol, followed by liquid paraffin, through the drainage tube into the common duct. By this method the retained stone may be partly dissolved and sufficiently fragmented so that it may be forced through the sphincter of Oddi when pressure is dammed up in the duct by temporarily clamping off the drainage tube. Further relaxation of the sphincter may be induced by amyl-nitrate inhalations or placing nitro-glycerine tablets beneath the tongue. Recently, I have had an opportunity to observe at St. Vincent's Hospital just such a case of a retained common duct stone that was partly dissolved by ether and alcohol injected through a drainage tube in the common duct and subsequently passed into the intestines. The same authors, Walters, Butsch and McGowan[5] have demonstrated that the normal intraductal pressure was 0 to 30 mm. of water, but that during attacks of biliary colic, the intraductal pressure frequently went as high as 160 mm. The use of opiates, especially morphine, tend to increase the intraductal pressure.

The use of sulfanilamide powder or any of its kindred preparations within the wound and especially about the drainage area of the common duct is recommended and urged. About 12 to 15 Gm. within the abdomen and about 3 to 4 Gm. scattered in the closure of the layers of the abdominal wall have been found to decrease the incidence of peritonitis and wound infections and predispose to a more uneventful recovery. The absorption of the drug from these areas seems to be relatively slow, for seldom was the Marshal test recording appreciably elevated.

COMPLICATIONS

After omitting all cases of catarrhal jaundice and its co-existing cholangitis, fifty-two cases of cholangitis were found to be present in this series of cases, and of these twelve died and twenty-three were operated upon. The remaining patients either refused operation or were treated by duodenal drainage, or symptomatically with surprisingly good results. The majority of these cases were associated with

cholelithiasis and cholecystitis. Various degrees of hepatitis, jaundice and biliary cirrhosis was recorded in many of the cases

tractions caused by previously impacted common duct stones may cause as great or greater trouble in the future than the

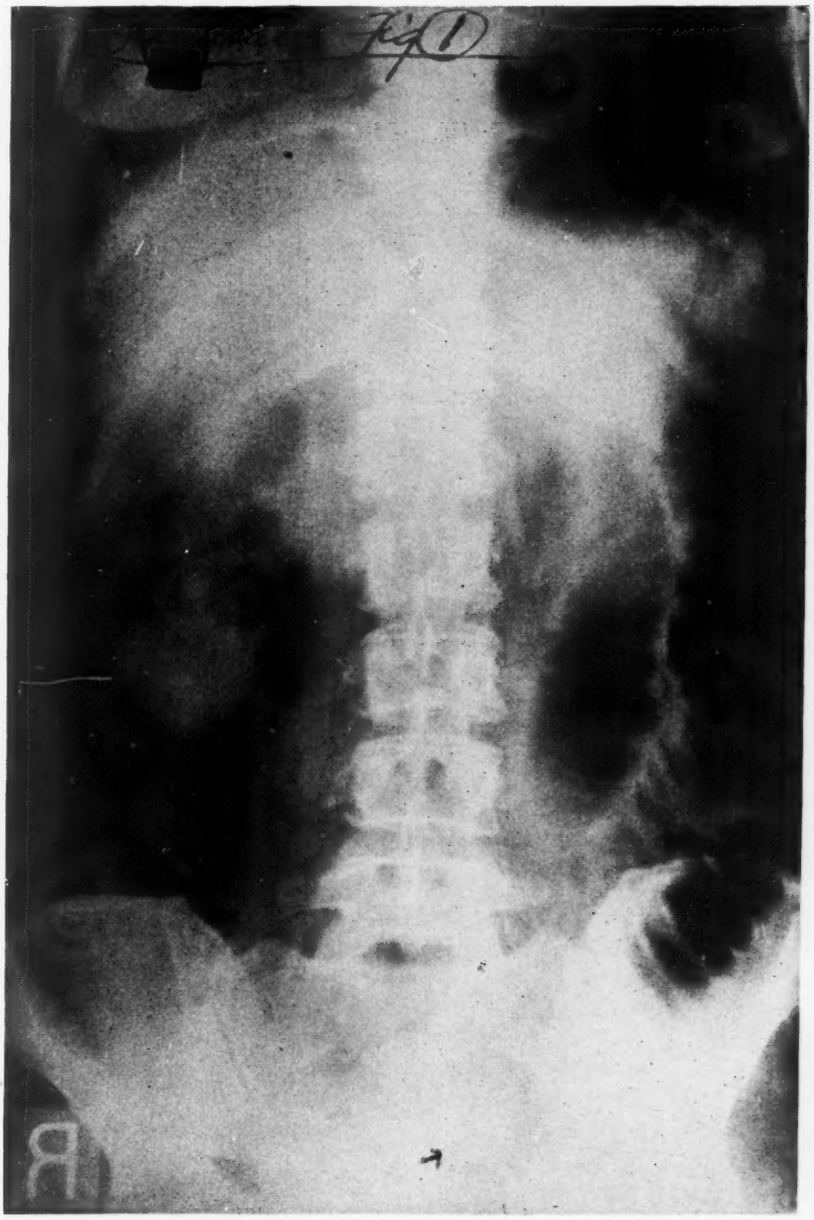

Fig. 1. Large gallstone in loop of small intestines in pelvis causing complete intestinal obstruction.

and fifty-one of the patients were found at the time of operation to be suffering from some degree of pancreatitis. Twelve cases of persistent external and two of duodenal-biliary fistulas have already been enumerated in the analysis of this series of cases.

Strictures, as a result of cicatricial con-

stones caused. Strictures also occasionally form at the site of exit of the "T" tube from the duct.

Impacted stones in the ampulla of Vater not infrequently cause pancreatitis as they either plug off drainage from the pancreatic duct of Wirsung or else dam up the

contaminated bile in the common duct and cause an overflow into the pancreas through its main duct.

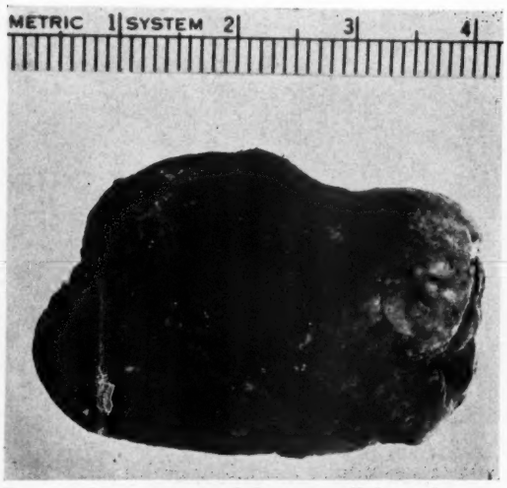

FIG. 2. Stone removed from small intestines at enterotomy.

Occasionally, gallstones of great size are passed through the ampulla or else through a fistulous tract between the gallbladder and the duodenum and cause a resultant intestinal obstruction. This obstruction occurs usually in the ileum or at the ileocecal valve and more rarely in the jejunum or the colon. One such patient with an obstruction of the ileum of long duration was operated upon by us two years ago. A short summary of the case with illustrations of the obstructing stone is presented (Figs. 1, 2 and 3):

CASE REPORT

A. L., aged sixty-two, a white female, was admitted to St. Vincent's Hospital by ambulance on August 19, 1939, complaining of sharp, cramp-like right upper quadrant pain, which radiated to her back, and was accompanied by nausea and vomiting. This present attack started four days before admission, but a similar attack associated with increasing weakness, an unproductive cough and alternating constipation and loose bowel movements manifested itself two weeks prior to admission. Her past history was negative except for dyspnea on exertion for the past two years.

On physical examination the temperature was 104°F., the pulse 126, blood pressure 140/86 and respirations 24. The patient was greatly dehydrated, and appeared acutely ill and very weak. No dyspnea and no jaundice were present. There were râles in both bases with

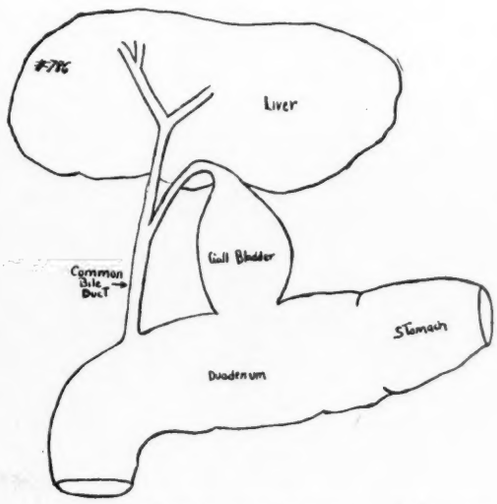

FIG. 3. Illustrates spontaneous cholecystoduodenal fistula through which gallstone entered intestines.

dullness and diminished breath sounds in the right lower lobe. The heart was slightly enlarged, was of regular rhythm and no murmurs were audible. The abdomen was distended and revealed no scars. There were no areas of tenderness and no palpable masses but there was shifting dullness in the flanks. Rectal and vaginal examinations were negative and there was no edema of the extremities.

Laboratory analyses of the urine disclosed a trace of albumen, and an occasional red blood cell and white blood cell. The red blood count was 5,000,000, the hemaglobin 94 per cent (13.5 Gm.), the white blood count was 7,160 and there were 86 per cent polymorphonuclear neutrophiles, 12 per cent lymphocytes and 2 per cent myelocytes. A blood culture taken a few hours after admission was negative.

X-ray examination of the abdomen revealed a large collection of gas in distended loops of the small intestine, particularly on the left side. There was a calcified mass in the left pelvic fossa which was below the level of the distended coils of intestines. This mass was believed to represent either a gallstone or a fecalith.

Diagnoses: Intestinal obstruction (small intestines), bronchopneumonia and arteriosclerosis. Operation was delayed long enough to attempt to re-establish her fluid and electrolyte

balance by intravenous medication and to decompress her distention by Wangensteen drainage.

Fig. 4. *X*-ray taken in original hospital prior to removal of gallbladder and stones in gallbladder and stone in the ampulla of Vater.

Fig. 5. Showing stone in ampulla of Vater that was not discovered at time of operation.

The abdomen was opened by a right rectus incision and no free fluid was found to be present. The small intestines were greatly distended and eighteen inches above the ileocecal junction a large spool-shaped mass was found to be impacted in the ileum and to be the cause of the complete obstruction. The mass could not be milked backward and was removed from the intestines by an enterotomy, and found to be a large gallstone which measured 4 by 2½ cm. The abdomen contained many adhesions in the right upper quadrant and the gallbladder could not be visualized. The abdomen was closed without drainage.

The patient died on August 20, 1941, twelve hours after operation. At autopsy no evidence of any leakage about the site of the enterostomy was found to be present, but a spontaneous cholecystoduodenal fistula with a large lumen existed. The cause of her death was believed to be overwhelming toxicity from an intestinal obstruction of four days' duration and her bronchopneumonia.

The following case history is one of a type that occurs all too often, namely, retained common duct stones after cholecystectomy. This particular patient had the good fortune to pass her stones into her intestines and avoid the hazardous experience of a second operation on her biliary system.

Mrs. V. B., a fifty-year old white lady was taken ill about March 1, 1939, at her home. She complained of pain and a marked soreness in her midepigastrium which were greatly accentuated when she stood upright. The pain radiated at times to both scapular areas and was occasionally accompanied by nausea and vomiting. After four weeks of symptomatic treatment with diet and sedatives by her local doctor, surgery was decided upon and she was hospitalized. Preoperative *x*-rays taken at that hospital revealed the presence of a large stone 2 cm. in diameter, and a smaller stone about 1 cm. in diameter in the area of her gallbladder. (Fig. 4.) However, there was a third stone visible in the *x*-ray at the level of the transverse process of the third lumbar vertebra that apparently escaped their attention. On April 4, 1939, she was operated upon and a huge hydrops of her gallbladder showing signs of ulceration and containing many stones was found. A cholecystectomy and an appendectomy were performed, and the operation report stated, "there were no stones in the common duct." The duct, however, was not opened and probed.

The patient states that following operation she never obtained complete relief from her "soreness in the epigastrium," but her wound healed well and she was discharged from the hospital on her twelfth postoperative day. She subsequently moved to New York City where she was first seen by me on April 24, 1939, about three weeks after her operation and a diagnosis of common duct stone was made. At this time she was markedly dehydrated, jaundiced and in severe pain. This pain radiated from her midepigastrium to her back and her two scapular areas. She was admitted to St. Vincent's Hospital the following day, April 25, 1939.

Fig. 6.

Fig. 7.

Fig. 8.

Figs. 6, 7 and 8. Illustrate relation of stone in common duct to the duodenum after administration of a bismuth meal.

At this time, the patient's jaundice, distress and pain had increased and her stools were light in color. The urine was amber in color and

positive for bilirubin and urobilinogen in dilutions of 1:10 but negative in dilutions of 1:20. Laboratory analyses of her blood revealed the following: (1) The red blood count was 3,630,000 with 78 per cent hemaglobin; (2) the white blood count was 11,750 with 87 per cent polymorphonuclears and a slight shift to the left; (3) her blood was type IV; (4) the blood sugar was 90 mg. and the nonprotein nitrogen was 27; (5) the icteric index was 43; (6) the Van den Burgh was 3-plus biphasic indirect (being 10 mg.). Flat *x*-rays of the abdomen revealed the presence of a rounded opaque body at the level of the right transverse process of the third lumbar vertebra. Confirmatory *x*-rays taken after ingestion of a barium meal again showed the rounded opaque body to occupy a position corresponding to the location of the ampulla of Vater. (Figs. 5 to 8.)

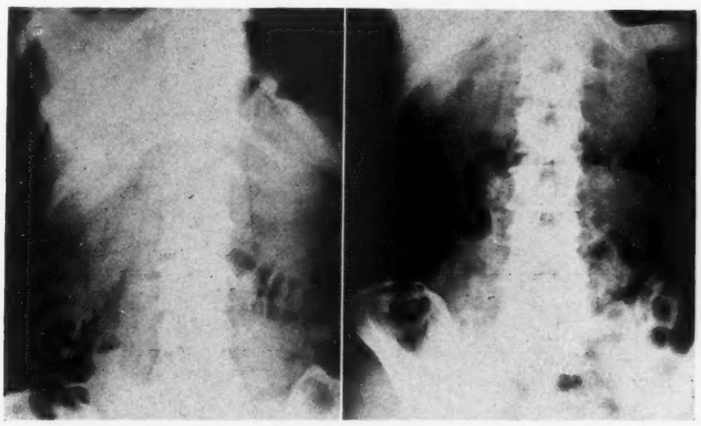

Fig. 9. Fig. 10.

Figs. 9 and 10. Illustrate stone in cecum after passing from the ampulla of Vater through the small intestines.

The positive findings of these *x*-rays, the elevated icteric index, the jaundice, and the persistence of pain across both low scapular areas and the midepigastrium, together with her nausea and vomiting confirmed the admission diagnosis of common duct stone following a cholecystectomy.

The method of treatment then had to be determined. The patient had been suffering marked pain for nearly two months and operation had given her little or no relief. She had lost her desire to live, was asthenic, a mild cardiac, dehydrated, and in the past several weeks had lost twenty pounds in weight. In brief, in her present condition she was only a fair surgical risk and if operation were to be performed considerable adhesions were to be expected because of the gangrenous areas reported as having existed in her massive gallbladder. Consequently, it was decided to make an attempt with the aid of certain medication to encourage the spontaneous passage of the stone. Accordingly, the following régime was instituted on April 29th: (1) bile salts gr. 10, three times a day with meals; (2) fatty meal at noon each day; (3) precede each fatty meal with atropine gr. $\frac{1}{150}$ (by hypo); (4) nitroglycerine gr. $\frac{1}{100}$ three times a day before meals; (5) allow patient up in chair; (6) no morphine unless pain is too severe to tolerate.

Atropine and nitroglycerine were administered in an effort to relax the obstructing contraction of the smooth muscle fibers in the duct and the sphincter of Oddi at the ampulla of vater. Nitroglycerine tends to relax or inhibit smooth muscle tissue directly, while atropine, a useful anodyne in gallstone colic acts on the nerve ends of the vagus nerve which supplies motor fibers to the biliary tract musculature and inhibitory impulses to the sphincter of Oddi permitting it to dilate. The "fatty meal" was given so that, whatever stimulation the duodenal hormone, "cholecystokinin," might exert on the biliary tract after the removal of the gallbladder, would be utilized to help evacuate the stone. Morphine was not prescribed except as a possible necessary analgesic because of its inhibiting effect on the rhythmic contractions of smooth muscles.

The efforts of the first day were unsuccessful, but on the second day the patient experienced an increase in her pain, an elevation of her temperature to (100.6°F.) and her pulse rate which previously had been between 70 to 80 rose to 100. Shortly thereafter the acute pain

in her epigastrium subsided and was replaced by a soreness while the pain in both scapular areas disappeared entirely. A check-up flat

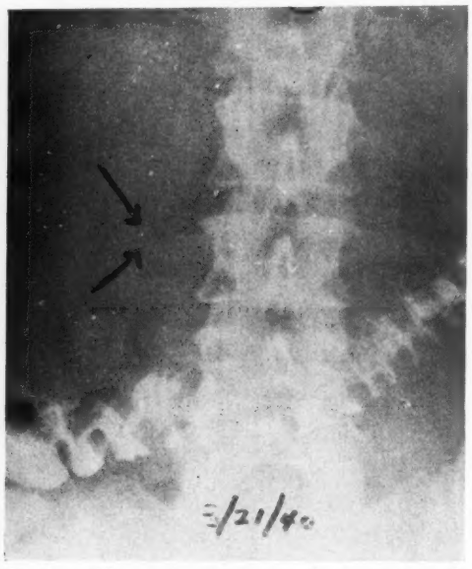

Fig. 11. Shows the presence of a new stone in the common duct one year later.

x-ray of the abdomen taken on May 1 and repeated the following day showed the stone to have passed into the large intestines. (Figs. 9 and 10.)

During the following days, the patient's clinical jaundice subsided, her icteric index fell to 19 on May 3, and all her pains and nausea disappeared. Her stools became brown in color, but the stone was not recovered from them. The patient was discharged from the hospital as cured on her twelfth hospital day. She was symptom free for the following seven months.

On January 15, 1940, she again appeared at my office complaining of occasional nausea and a return of pain in her midepigastrium which pain radiated to her right flank and scapular area and less so to her left flank and scapula. This pain seemed to her to be different in character to her previous pains. The pain had manifested itself on only five or six occasions in the past three weeks, and she attributed it to having eaten too heavily during the Christmas and New Year holiday season. Although she had gained two pounds in weight, she felt generally poor and had been troubled with sluggish bowels and abdominal distention, which was not accompanied by either belching or the passing of flatus. *X*-rays of the stomach and intestines revealed no pathological condition but did reveal a dense shadow in the right side of the abdomen that was believed to represent a moderately enlarged right hepatic lobe. The suspicions of the existence of an ulcer unconfirmed, the possibility of a recurrence of the chronic pancreatitis which she was reported as suffering from at time of operation was considered and an analysis of her blood showed the "amylase" content to be 182 units (normal 70 to 200) and the urine amylase to be 170 units, also within normal range. Her pain for forty-eight hours after the gastrointestinal series was unrelenting. She was nauseated and vomited. Her temperature and blood count were relatively normal and her icteric index was 7.5. Multiple *x*-rays taken of the "biliary tree" (flat plates and a keraphen series) failed to disclose any evidence of a calculus or a distended common duct. However, the colon enema series that revealed a mild colitis, did reveal evidence in one film that was strongly indicative of a new common duct stone. This shadow was located exactly where her previous common duct stone shadow was located at the tip of the right transverse process of the third lumbar vertebra. (Fig. 11.)

This second stone although smooth, oval and apparently solitary, cast a different type of shadow from the stone of a year ago. This second stone's shadow was "signet ring" in type and probably was formed by deposition of layers of cholesterol, pigment calcium and calcium carbonates. The shadow cast in the films of the previous solitary stone although also oval and smooth, was solid and dense, and was probably a so-called "combined calculus" formed by a radial cholesterol calculus with a laminated cholesterol calcium covering.[33]

Since this shadow of a stone was not present after her attack subsided several months ago, and since the patient has been entirely well and symptom free for the seven months prior to January of this year, it is interesting to speculate where the stone was formed. Did it form in a branch of the right hepatic duct and cause the resultant swelling of the right lobe of the liver, or could there have been a spasm of the sphincter of Oddi in the ampulla with a resultant stasis and dilation of the common duct with bile elements and infection piling up a new stone? The latter of the two is more probable. As the patient was free from signs of a clinical jaundice, the icteric index was low and the pain was irregular in time and duration, it was probable that this stone was not wedged in the

ampulla like the previous stone, but rather was acting like a ball valve. The patient requested that surgical intervention be postponed until after another attempt had been made to pass the stone with the aid of medication. A trial period of medication as previously described was instituted and following this the patient was unusually free from pain and felt better for four days.

However, on the fifth day, the patient was suddenly seized with a very severe attack of pain in her right upper quadrant and mid-epigastrium that prostrated her. This pain radiated to both her back and right scapular area and was relieved only after the administration of morphine and atropine hyperdermically. The acute pain disappeared within a few hours just as suddenly as it had come. During the following twenty-four hours the patient had a mild degree of soreness in her epigastrium, and on the following day she was discharged from the hospital symptom free.

In the month following her discharge from the hospital she gained twelve pounds in weight. Her medication of bile salts was continued, her diet was only slightly restricted and the enlarged right lobe of the liver shrunk in size. She was observed by me at frequent intervals for a year after her discharge and she had no recurrence of her previous acute distress and vomiting.

It is too much to expect that all such cases could have such a successful and non-surgical ending, but in this case and in two other cases that have since come under my observation, patients have successfully passed a retained common duct stone after instituting this method of treatment. However successful this method may be in some cases in assisting in the passage of a common duct stone, it must be borne in mind, that some degree of infection of the bile in the duct usually exists wherever a stone is present, and that this method does little to improve the infection.

CONCLUSIONS

1. Common duct stones are very frequently present in cases of cholecystitis and pancreatitis and should be carefully searched for. The high incidence of choledochol stones is substantiated by findings in a review of the recent literature.

2. Criteria for drainage of the common duct are, the presence of infection or stones in the duct, dilatation of the duct, the aspiration of murky bile from the duct, or the existence of pancreatitis or jaundice, together with a persistent high pulse rate in spite of adequate sedation. To these most surgeons would also add a small contracted gallbladder or multiple small stones within it.

3. Since infection and calculi of the common duct are nearly always secondary to cholecystitis, the internist is urged not to delay in the transfer of such a patient to a surgeon. The internists who treat these patients first usually have the opportunity to see that surgery is instituted before liver and common duct damage occurs.

4. Surgery should not be hasty nor should it be delayed unnecessarily. Before attempting surgery, the electrolyte balance should be re-established and in jaundice cases, vitamin K should be given in ample dosage.

5. When a duct is opened, it should be carefully probed before inserting a drain and suturing the incision in the duct about it. Sulfanilamide powder (12 Gm.) should be scattered about the duct and in the abdominal wound.

6. The failure of relief from symptoms following a cholecystectomy or a choledochostomy is usually indicative of a stone that was overlooked. Such pain is usually of organic rather than of functional origin.

7. The nitrites (amyl-nitrate and nitroglycerine) have a relaxing influence on the sphincter of Oddi and help facilitate the passage of a retained stone. Opiates, especially morphine, tend to increase the intraductal pressure.

8. A case history of a patient, who following medication with nitrites, atropine and bile salts spontaneously passed two retained common duct calculi was cited.

9. Gall bladder disease and cholelithiasis are rare among people of the colored race. Compared to the white race, the incidence

is one-twentieth as great. The occurrence of gallstones in many cases of sickle cell anemia was noted.

10. An analysis of 2,602 cases of biliary tract disease was presented. Biliary calculi were found in over 47.2 per cent of the 2,548 cases of cholecystitis among 250,065 hospital admissions during the past ten years at St. Vincent's Hospital and Harlem Hospital. Nine per cent of those who had stones, had their stones in the common duct, but only 5.5 per cent of the patients with gallbladder disease who were operated upon had stones recovered from their common ducts, and 6.6 per cent had their ducts opened and drained. Fifteen hundred seventy-five of the total cases were operated upon.

11. There is some similarity in incidence of common duct surgery and common duct stones in the 4,881 operative cases of cholecystic disease comprised of the series of 3,306 operative cases of gallbladder disease on the surgical service of Post-Graduate Hospital, in seventeen years reported by Heyd and Hotz[13] and the 1,575 cases of cholecystic disease on the surgical service of St. Vincent's and Harlem Hospitals in the past ten years. These figures differ greatly from the statistics of other authors who report a much higher incidence of common duct drainage and stones.

12. This low incidence of common duct stones probably may be attributed to the fact that the common ducts were opened and probed in such a small percentage of cases. Those patients seen in the follow-up clinics, who still complain of pain persisting in the right upper quadrant following cholecystectomy are possibly bearing pain from stones that were inadequately searched for, or from chronic infections of the common duct which were not recognized.

13. Surgery of the gallbladder and bile ducts without becoming audacious should, it would seem, become less conservative but more thorough and radical. The percentage incidence of common duct stones varies in proportion to the number of common ducts which are drained. An analysis of over 9,272 operative cases of cholecystitis reported in the literature bears proof of this assertion.

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DIFFUSE hypertrophy (of the female breast) is of a progressive nature, the growth being either rapid or slow, and with little or no tendency to spontaneous cure. In cases of virginal hypertrophy, arrest of this condition is rare.

MORTALITY RATE FROM ACUTE APPENDICITIS IN A MUNICIPAL HOSPITAL

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THE high incidence of death from appendicitis in the United States has made the management of this disorder of the greatest importance to all members of the medical profession. Especially is it of concern to surgeons, to whose care the majority of cases are usually consigned. In 1939, in the United States appendicitis stood fifteenth as the cause of death with 14,113 fatalities.

All factors concerned with the incidence, the onset and the treatment of this disorder are matters for pertinent investigation. In an attempt to throw further light on the morbidity and mortality factors concerned in this disease we have investigated carefully 677 cases of acute appendicitis and its complication in which the patients have been operated upon on the Fourth Surgical Division of Bellevue Hospital in New York City. This study covers the years 1928 to 1939 inclusive and includes only proved cases of acute appendicitis. All subacute, chronic, recurrent and mechanical disorders were eliminated.

The surgical approach will be discussed in some detail later. In general it consisted of immediate operation, adequate exposure, generally through rectus splitting incisions, protection of adjacent bowel from contamination and drainage of the abdomen when indicated.

Mortality Rates. From 1928 through 1939, 677 patients with acute appendicitis followed by various complications, have been operated upon on the Fourth Surgical Division at Bellevue Hospital. These cases have been subdivided into acute appendicitis, localized peritonitis, abscess and spreading or general peritonitis. As the differentiation at operation between localized and spreading peritonitis is inaccurate at best, these two groups have also been considered as one. In none of these cases reported was sulfanilamide given intraperitoneally or orally. An analysis of the mortality in these cases is given in Table 1.

TABLE 1
MORTALITY FROM APPENDECTOMIES, 1928 TO 1939

Diagnosis	No. Cases	No. Deaths	Deaths, Per Cent
Acute appendicitis	474	8	1.6
Local peritonitis	67	4	5.9
Abscess	88	7	7.9
General peritonitis	48	16	33.3
All peritonitis	115	20	17.3
Total	677	35	5.1

Further investigation of these cases revealed that there had been a surprising drop in the mortality of the cases during the latter half of this twelve-year period. This is evident from a glance at Table II in which comparison is made between the 1928 to 1933 and the 1934 to 1939 periods. It will be noted that the mortality rate dropped in the second period to nearly half of that in the earlier period (6.3 to 3.4 per cent). The greatest rate of decrease was in the acute cases but the decrease in the percentage of deaths was also very marked in the cases of general peritonitis.

Two important reports have recently appeared on the mortality rate in appendicitis. Reid and Montanus[1] gave data on 1,153 cases treated at the Cincinnati General Hospital from 1934 to 1938 inclusive. Haggard and Kirtley[2] summarized the reports on 2,777 cases treated from 1919 to

1935 in the hospitals of the University of Minnesota, the University of Michigan, the University of Iowa and Vanderbilt University. These reports together with the mortality rate include 232 cases of chronic appendicitis with only one death. If this group is excluded from their total, it is found that they had fifty-five deaths in 921

TABLE II

COMPARISON OF MORTALITY IN 1928 TO 1933 PERIOD WITH THAT IN 1934 TO 1939 PERIOD

Diagnosis	1928 to 1933			1934 to 1939		
	No. Cases	No. Deaths	Deaths, Per Cent	No. Cases	No. Deaths	Deaths, Per Cent
Acute appendicitis	266	7	2.6	208	1	0.47
Local peritonitis	33	2	6.06	34	2	5.8
Abscess	69	6	8.6	19	1	5.2
General peritonitis	23	10	43.4	25	6	25.0
All peritonitis	56	12	21.5	59	8	13.5
Total	391	25	6.3	286	10	3.4

data from Bellevue Hospital are given for comparison in Table III.

A glance at these figures shows that the mortality rate at Bellevue Hospital compares most favorably with those obtained in the large teaching hospitals throughout the country, this is especially evident for the period 1934 to 1939, the average mortality rates being definitely lower for

TABLE III

COMPARISON OF MORTALITY STATISTICS AS REPORTED FROM SEVERAL LARGE HOSPITALS

Diagnosis	Average Four Hospitals (Haggard and Kirtley), Per Cent	Cincinnati General Hospital (Reid and Montanus) Per Cent	Bellevue Hospital		
			1928 to 1939, Per Cent	1928 to 1933, Per Cent	1934 to 1939, Per Cent
Acute appendicitis	0.49	1.03	1.6	2.6	0.47
Abscess	6.3	10.08	7.9	8.6	5.2
Local peritonitis	7.7	.....	5.9	6.06	5.8
General peritonitis	41.2	.....	33.3	43.4	25.0
All peritonitis	.....	17.22	17.3	21.5	13.5
Chronic appendicitis	.....	0.43			
Total	5.5	4.86	5.1	6.3	3.4

Bellevue. Moreover, Reid and Montanus, whose data cover approximately the same period (1934 to 1938) in computing their cases, or an average mortality rate of 5.97 per cent.

Effect of Mortality Rate of Experience of the Operator. Haggard and Kirtley quote Bowers to the effect that "The mortality from appendicitis decreases with the experience of the surgeon." Detailed investigation into the experience of the operators attending these 677 cases at Bellevue presents no data to warrant any such assumption in these cases. No increased experience by members of the surgical staff was responsible for the decrease in mortality, for only two of these operations were performed by the full attending and very few by the associate attending surgeons.

On the contrary, the operations were performed in two-thirds of the cases by the house staff who had had at the most two years of surgical training. Indeed one-third of the house staff had had only eighteen months' training. These relatively inexperienced men numbering seventy-two, performed 410 of the 677 operations with a mortality of only 3.4 per cent. The remaining 267 cases with a mortality rate of 7.8 per cent were operated upon by twenty-eight members of the attending staff. Obvi-

ously, the attending staff operated upon the more seriously ill patients.

From these data it is evident that no increased surgical skill was responsible for the decrease in mortality.

Sex and Age of Patients. Our data show that appendicitis was more common among males than females. Of our 677 cases 465 were men and 212 women.

As is shown in Table IV, appendicitis is far more frequent in the second and third decades of life than in later years. In all, 208 cases were in the twelve to twenty-year group and 225 cases in the twenty to thirty

TABLE IV
AGE OF PATIENTS BY DECADES

Diagnosis	12–20	20–30	30–40	40–50	50–60	60–70	Over 70
Acute appendicitis	163	171	81	40	16	3	1
Local peritonitis	17	22	8	11	5	0	3
Abscess	17	22	18	17	9	0	3
General peritonitis	11	10	6	10	5	5	0
Total	208	225	113	78	35	8	7

year group. The incidence of the disease became progressively less as the age increased. No children under twelve years are included in this material as these patients are cared for on the Children's Surgical Service

History of Previous Attacks. In Table V are given data concerning the history of previous attacks of appendicitis.

TABLE V
HISTORY OF PREVIOUS ATTACKS

Diagnosis	No. of Cases	Per Cent
Acute appendicitis	114	24.05
Local peritonitis	16	23.8
Abscess	12	13.6
General peritonitis	13	27.08

It appears from these figures that approximately one-fourth of the patients operated upon had suffered from previous attacks of the disease.

Duration of Symptoms. In order to determine whether the duration of symptoms played a rôle in the difference in mortality rates between the two groups of cases an analysis was made of this factor. These data are presented in Table VI.

TABLE VI
DURATION OF SYMPTOMS

Diagnosis	1928 to 1933	1934 to 1939
Acute appendicitis	39 hr.	29 hr.
Local peritonitis	54 hr.	48 hr.
Abscess	5.6 days	10.2 days
General peritonitis	52 hr.	56 hr.

From this table it is to be noted that there was a definite shortening of time between the development of the symptoms and operative intervention in the cases of acute appendicitis. Reid and Montanus report a similar decrease. It may possibly play a rôle in the decreased mortality of this group.

In the cases of abscess the duration of symptoms is nearly doubled in the later group, the duration of 10.2 days, on the average, as compared with 5.6 days in the earlier group. Haggard and Kirtley believe that abscesses operated upon during the third, fourth or fifth day, at the height of the attack, result in a very high death rate. This statement is apparently borne out by our figures, from which it may be seen that the death rate from abscess in the earlier six-year period with a duration of symptoms of 5.6 days was 8.6 per cent as compared with 5.2 per cent during the period in which the average duration of symptoms was 10.2 days. Reid and Montanus, who reported that in abscesses the elapsed time between symptoms and admission to the hospital was 129.6 hours for the 1915 to 1933 period and 145.9 hours for the 1934 to 1938 period, also had a slightly decreased mortality for the longer time—10.08 per cent for the later period as compared to 11.4 per cent for the earlier one.

No marked difference in the duration of symptoms was seen for either local or general cases of peritonitis. In the former instance the length of time during which

symptoms were present dropped from fifty-four to forty-eight hours. The mortality rate likewise dropped from 6.06 to 5.8 per cent. This difference is so small as to be immaterial. In the cases of general peritonitis the average duration of symptoms increased from fifty-two to fifty-six hours. The mortality, however, dropped from 43.4 to 25 per cent. It is evident that the decrease in mortality in the cases of peritonitis cannot be ascribed to any change in the length of time during which the symptoms were present before the patients presented themselves for treatment.

TABLE VII
HISTORY OF ADMINISTRATION OF CATHARTICS

Diagnosis	One Cathartic	Two or More Cathartics	Enema	Cathartic and Enema	Total
Acute appendicitis	95	23	28	23	169
Local peritonitis	18	7	9	5	39
Abscess	13	12	9	5	39
General peritonitis	14	5	3	0	22
Fatalities	7	5	4	1	17

Catharsis. Many papers have been written on the dangers of administering laxatives to patients suffering from appendicitis. Concerted efforts have been made from time to time to acquaint the public with the dangers of taking such medicaments for supposed attacks of "indigestion" which may, in reality, be attacks of appendicitis. Less generally admitted by the medical profession is the fact that physicians are themselves not free from criticism on this score. In our series, seven patients had taken cathartics on the order of the physician. Fortunately, none of these patients had fatal outcomes. Reid and Montanus reported that cathartics had been prescribed by physicians in twelve of their 1,153 cases.

The cathartic history of our cases is presented in Table VII.

In our entire series of 677 cases there were thirty-five fatalities. As may be seen from the above table, seventeen of these were associated with the administration of cathartics and enemas. Omitting from consideration the four cases in which enemas alone were given, thirteen fatalities were associated with cathartics. On the other hand, twenty-two patients died who had been given none. From these figures we are unable to draw any definite conclusions as to the rôle of cathartics in deaths from appendicitis.

Operative Procedure. Does the type of operative procedure have any effect on the mortality in cases of appendicitis? Incisions are always cited as a factor in mortality. There is a general concensus of opinion that the McBurney incision is associated with a much lower morbidity and mortality. The type of operative procedure used and the mortality ensuing have been analyzed for our two series of cases in Tables VIII and IX. It will be seen that the mortality for the McBurney incision is lower than that from the rectus incision, but the number is so small that a fair comparison is impossible.

TABLE VIII
OPERATIVE PROCEDURE—1928 TO 1933

Diagnosis	Right Rectus Incision			Kam. Incision			McBurney Incision		
	No. Cases	Deaths	Per Cent	No. Cases	Deaths	Per Cent	No. Cases	Deaths	Per Cent
Acute appendicitis	246	7	2.8	11	0	0	9	0	0
Local peritonitis	32	2	6.2	0	0	0	1	0	0
Abscess	62	6	9.6	2	0	0	5	0	0
General peritonitis	21	10	47.6	1	0	0	1	0	0
All peritonitis	55	12	22.6	1	0	0	1	0	0

TABLE IX

OPERATIVE PROCEDURE—1934 TO 1939

Diagnosis	Right Rectus Incision			Kam. Incision			McBurney Incision		
	No. Cases	Deaths	Per Cent	No. Cases	Deaths	Per Cent	No. Cases	Deaths	Per Cent
Acute appendicitis	138	1	0.7	8	0	0	70	0	0
Local peritonitis	27	2	7.4	0	0	0	7	0	0
Abscess	13	1	7.6	0	0	0	5	0	0
General peritonitis	19	1	5.2	0	0	0	2	1	50
All peritonitis	46	3	6.08	0	0	0	9	1	11.1

It may, however, be of some significance in the decreased mortality found during the later period, that the number of McBurney incisions has increased and the number of right rectus incisions has correspondingly decreased. This is especially evident in the cases of acute appendicitis. During the period, 1928 to 1933, 246 right rectus incisions were made for acute appendicitis and only nine McBurney incisions. During the 1934 to 1939 period 138 right rectus incisions were made for acute appendicitis and seventy McBurney incisions. It must, however, be emphasized that during the later period the mortality from the right rectus dropped markedly—from 2.8 to 0.7 per cent. Greatly decreased mortality was also evident during the later period from the right rectus incision in cases of general peritonitis.

TABLE X

TREATMENT OF APPENDICEAL ABSCESS (EIGHTY-EIGHT CASES)

Treatment	No. Cases	Per Cent of Total	Deaths	Mortality Rate
Appendectomy	66	75	4	6.2
(partial removal)	(4)	(6.2)	(0)	(0)
Drainage only	22	25	3	13.6

The type of incision is of added significance if we consider the mortality of general peritonitis operated upon under the mistaken diagnosis of perforated peptic ulcer. Here the mistaken diagnosis and the inappropriate incision prove to be a lethal factor, even if subsequently the McBurney incision is made. If doubt is present as to the presence of a perforated appendix, it certainly appears justifiable to uncover this

TABLE XI

DRAINAGE AS PART OF OPERATIVE PROCEDURE

Diagnosis	1928 to 1933				1934 to 1939			
	Peritoneal Drainage		Mural Drainage		Peritoneal Drainage		Mural Drainage	
	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent
Acute appendicitis	74	27.8	42	15.7	23	11.3	45	21.6
Local appendicitis	29	87.8	2	6.06	26	76.4	5	14.7
Abscess	68	98.8	0	0	19	100	0	0
General peritonitis	22	95.6	1	4.0	25	100	0	0

area first with a McBurney incision. The production and closure of such an incision, if done mistakenly, does not place the operator in the position of being unable to retrieve a difficult situation, such as is present when the abdomen has been invaded and explored through an upper right rectus incision.

The management of eighty-eight cases of appendiceal abscess is given in Table x.

From these figures it appears that somewhat better results were obtained when removal rather than drainage alone was undertaken.

The rôle played by drainage and particularly the type of drainage is also of interest in any discussion of the operative treatment of appendicitis and the treatment of its complications. The number of cases in which drainage was used and the type of drainage is given in detail in Table xi.

From these figures it appears that peritoneal drainage has been somewhat less popular during the later than during the earlier period investigated, and that mural drainage has become more generally used than formerly. We do not believe, however, that this difference in treatment has any material effect upon the mortality rate.

Table xii
PREOPERATIVE COMPLICATIONS

Diagnosis	No. of Cases	Mortality
Small bowel obstruction by abscess	1	0
Pulmonary tuberculosis	4	0
Uncontrolled diabetic acidosis	2	1
Otis media bilateral	1	0
Cellulitis of scrotum	1	0
Gonococcal urethritis	2	0
Catheter lost in bladder before operation	1	0
Leuetic aortitis and hypertension	1	0
Asthma	1	0
Acute appendicitis in incarcerated hernia c. ileus	1	0

Preoperative Complications. Our series of cases were attended by a number of complicating factors which are listed in Table xii. This table needs no further discussion. The number of cases in each classification is too small to allow conclusions to be drawn.

Table xiii
POSTOPERATIVE COMPLICATIONS

Condition	No. Cases	Mortality	Comments
Pregnancy	5	1	3 aborted, 1 with fatal hemorrhage
Pelvic abscess	8	0	7 subsided, 1 drained spontaneously
Fecal fistula	10	0	4 closed at operation 6 closed spontaneously
Dehiscence	10	2	1 sutured, 9 packed
Ventral hernia	7		
Subphrenic	2	1	1 died, rupture into chest 1 recovery, drainage
Phlephlebitis	2	2	
Gas infection abdominal wall	2	1	
Pneumonia	15	0	
Wound infections	71		
Hematoma	6		
Postoperative hemorrhage	4	1	
Retained appendices, drainage	7		
Obstruction	2	0	
Embolus	2	1	
Abscess of abdominal wall	1	1	
Atelectasis	4	0	
Phlegmon of abdominal wall	1	1	
Delirium tremens	1	0	
Tonsillitis and pharyngitis	8	0	
Phlebitis	3	1	
Fall out of bed, 1 hour postoperatively	1	0	
Abscess of L O I H sac, abscess	1	0	
Perirectal abscess	1	0	
Cellulitis of hand	1	0	
Urethral stricture, dehiscence	1	1	
Epileptic convulsions	1	0	
Cystitis	1	0	
Bronchitis	1	0	
Acute rheumatic carditis	1	0	
Abscess of back	1	0	
Cardiac decompensation and fibril	1	0	

Postoperative Complications. The postoperative complications are listed in Table XIII. From this table it will be seen that wound infections were comparatively common, occurring in seventy-one of the 677 cases or in approximately 10 per cent. Aside from this complication the table speaks for itself. Only rarely was the postoperative complication associated with a fatal outcome.

Causes of Death. The causes of death are listed in Table XIV. The predominating cause of death was peritonitis; this accounts for twenty-seven of the thirty-five fatalities. Pneumonia was purposely omitted, as we believe it is of only secondary importance as a terminal manifestation. All fatal cases bear the inevitable note concerning the physical signs to be found in the lungs, and it is interesting to note that these can dominate the postoperative picture to such an extent that the mild abdominal distention present is ascribed to the pneumonia process. Autopsy quickly apprises us of the true situation. It seems safe to assume that control of the ileus in peritonitis by intubation has been a factor in reduction of mortality.

TABLE XIV
CAUSES OF DEATH

Cause of Death	No. Cases
Generalized peritonitis	27
Embolism or aspiration during lavage	1
Pylephlebitis	2
Subphrenic abscess	1
Postoperative hemorrhage	1
Shock	1
Small bowel obstruction	1
Postabortal uterine hemorrhage	1

Diagnosis and Its Difficulties. The diagnosis of appendicitis is not always a simple matter. This was called emphatically to our attention by one of our cases at Bellevue. The patient was watched on the ward for a suspected appendicitis for four days. Operation was determined upon only when signs of peritonitis appeared. The outcome, unfortunately, was death.

It is well enough to warn the public of the danger of appendicitis, and to attempt to educate them to call their physician promptly in attacks of abdominal pain. But what happens when they do call us? Have we clearly in mind the diagnostic criteria of the disease or will we, as was the case in the patient mentioned above, find ourselves unable to make a definite diagnosis until it is too late for successful operative intervention?

The classic textbook picture of the physical findings in acute appendicitis are not those of early appendicitis. Delay, waiting for spasm and rebound tenderness to appear, will result in a large percentage of cases of peritonitis. It is essential that we remember the mechanism of production of peritoneal pain and muscle spasm in appendicitis, and stress the fact that these are produced only when peritoneal involvement has begun.

Symptomatology may be an important factor in mortality statistics. It is apparent, on reviewing our case histories, that it was not pain that drove a patient to the hospital but the onset on nausea and vomiting. This is borne out especially in the cases of abscess and peritonitis. In many instances, these patients were able to go about their work and do everything they normally did. The only departure from normal was a mild ache in the right lower quadrant. This discomfort was not sufficient to drive the patient to a doctor. Immediately, however, when vomiting began and general discomfort became great, medical advice was sought.

A review of individual case histories plainly demonstrates that little diagnostic reliance could be placed on the patient's history, which in many instances is bizarre, to say the least, due to his etiological concept of the disease. In 15 per cent of the cases it was believed that the disorder started with a dietary indiscretion. In shifting the wheat from the chaff in the patient's history it is essential to remember that pain precedes nausea and vomiting, and to try to elicit the facts on these points out of the patient's vagueness. When there has been dietary indiscretion, nausea almost always precedes abdominal pain.

Physical Signs. Physical signs require careful evaluation to make an early diagnosis. It can be seen in Table xv that classic textbook physical signs of tenderness, spasm and rebound tenderness are present in only slightly more than 30 per cent of our cases. This means careful attention must be given to the patient with abdominal tenderness regardless of the luck

Table xv
PHYSICAL SIGNS

Physical Signs	No. Cases	Per Cent
Tenderness alone	152	22.4
Tenderness and rebound tenderness	107	15.7
Tenderness and rigidity	204	30.1
Tenderness, spasm, rebound tenderness	212	31.3
Palpable abdominal mass	58	8.5
Rectal tenderness	332	47.5
Negative rectal examination	162	23.9
Rectal not done	183	27.0

of corroborative inflammatory signs. Although these signs in general parallel the severity of the underlying process, it is worth noting that a spreading peritonitis may be present without abdominal signs other than tenderness. This situation was present in patients presenting themselves late in the disease with marked toxemia and dehydration.

Attention is called to the fact that a palpable mass is not necessarily a sign of abscess, it being present in twelve acute cases, six cases with local peritonitis and five with general peritonitis. A mass was actually palpable in only thirty-five of the eighty-eight appendiceal abscesses proved by operation, an incidence of 39.7 per cent.

Rectal tenderness as the table indicates was present in almost half of the cases. It is worth pointing out that in three of the cases of abscess the mass was palpable only by rectum.

Diagnostic Value of Leucocyte Count. The leucocyte count is properly held as only a minor diagnostic aid. This is borne out in our series of cases; the average results are presented in Table xvi. The

Table xvi
LEUCOCYTE COUNT (AVERAGE)

Diagnosis	Leucocytes	Polymorphonuclears, Per Cent	Normal, Per Cent
Acute appendicitis	14,400	84	14.8
Local peritonitis	16,200	86	9
Abscess	15,900	84	12.7
General peritonitis	15,300	85	23.4

average blood count was definitely increased in all classes of cases, but the amount of increase was not very great. Moreover, in a number of cases the blood count was normal, as shown in the last column of the table.

We believe that it is especially significant that of the sixteen patients who died of general peritonitis, six had normal leucocyte counts. We are also of the opinion that in such instances this laboratory test is of definite prognostic value.

Diagnostic Value of Patient's Temperature. As a diagnostic aid, the temperature is no surer criterion than the leucocyte count, as is evident from Table xvii. True the temperature in all classes of cases does show an increase, rather marked in the cases of general peritonitis. Unfortunately, however, from a diagnostic viewpoint, from

Table xvii
AVERAGE ADMISSION TEMPERATURE

Diagnosis	Average Temperature, °F.	Normal, Per Cent
Acute appendicitis	100.8	15.5
Local peritonitis	100.9	10.6
Abscess	100.9	11.4
General peritonitis	101.3	15.5

10.6 to 15.5 per cent (depending on the type of case) had perfectly normal temperatures.

Diagnostic Value of Pulse Rate. From Table xviii it is evident that the pulse rate cannot be taken as a significant diagnostic factor in appendicitis. Indeed, in approxi-

TABLE XVIII
AVERAGE PULSE RATE

Diagnosis	Pulse Rate	Below 90—Per Cent of Cases
Acute appendicitis	94	28.6
Local peritonitis	99	22.3
Abscess	98	19.3
General peritonitis	98	25.0

mately one-fourth of the cases the pulse was below ninety. The average pulse rate in all classes of cases was below 100.

Question of Conservatism in Appendectomy. The question has arisen during the past decade as to the advisability of conservative management in the late cases of appendicitis. Many authors report significant decreases in mortality with these measures. In reviewing our material it is difficult to formulate criteria for selection of these cases. The presence or absence of a mass has particularly been studied as a possible indicator of a localized process. It is important, however, to note that only 39.7 per cent of our appendiceal abscesses presented masses at the time of admission. The temperature likewise is not of help in the making of a decision to procrastinate. Many of our acute cases presented themselves with temperatures over 102°F., the underlying factor in these instances, apparently, being dehydration and acidosis. We, however, tend toward immediate operation with fluid administration by vein during the immediate preoperative and operative period. It is evident from our material that acute cases would have gone on to peritonitis had some of the so-called indications for conservative management been employed.

COMMENT

From our investigation of 677 cases of acute appendicitis and its complications as treated surgically at Bellevue Hospital, we have reached the conclusion that the lessened mortality which has been evident in later years is due not to any improvement in surgical technic but to the better general management of these cases. We attribute the lowered mortality rate to the universal use of parental fluids, to the use of blood transfusions and to the excellent work performed by the Department of Anesthesia.

When this statistical review was started, it was our purpose to analyze all pertinent facts pertaining to acute appendicitis and its complications. There were no preconceived ideas as to the management of any phase of the disease and it is interesting when all the data have been analyzed that no one method of attacking this disease could be given credit for our favorable results.

CONCLUSIONS

1. It would seem that the mortality in this series should represent the mortality for acute appendicitis throughout the United States in view of the fact that the 677 operations were performed by 100 different surgeons, seventy-two of whom were members of the house staff, who performed two-thirds of the total.

2. Although sulfonamide compounds have lowered the mortality in acute appendicitis, it played no part in this series as the study was concluded before the drugs were used.

3. Surgical delay in cases of abscess seems indicated from this study, but the diagnosis of an abscess is most difficult. In the eighty-eight cases it was diagnosed preoperatively in 39.7 per cent.

4. Removal of the appendix or simple drainage in the cases of abscess is still debated. In this series of eighty-eight cases twenty-two were drained with a 13.6 per cent mortality and sixty-six had an appendectomy with a 6.2 per cent mortality.

5. Nausea and vomiting are more important symptoms than pain in causing the patient to seek medical aid.

6. Tenderness and rigidity was present in only 30.1 per cent of the 677 cases and rectal tenderness in 47.5 per cent.

7. The leucocyte count is of limited diagnostic aid, and 14.8 per cent of the acute cases, 9 per cent of local peritonitis, 12.7 per cent of abscesses, and 23.4 per cent of general peritonitis revealed a normal count.

8. The temperature may be misleading in acute appendicitis as in 10.6 to 15.5 per cent the different types of the disease revealed a normal reading.

9. The pulse in this series was below 90 in 25 per cent of the total cases.

10. To assume that the lowered mortality of acute appendicitis in any institution in recent years is attributable to any one factor is probably erroneous.

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The term "gynecomastia" signifies the abnormal development of the male breast. True gynecomastia is a physiological phenomenon characterized by a non-painful and non-inflammatory growth which presents to the touch the characteristic lobulation of the female organ.

NONSPECIFIC MESENTERIC LYMPHADENITIS

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DESPITE the increasing interest in mesenteric lymphadenitis, the majority of discussions of the differential diagnosis of abdominal pain, including medical teaching, textbooks and current literature, consider only briefly or neglect the subject entirely. The papers by McLaughlin and Davis and by Ochsner and Murray are noteworthy exceptions. Because of the frequency of mesenteric lymphadenitis, its questionable etiology, and the difficulty of differentiation from acute appendicitis, we believe the subject cannot be emphasized too often. In 1939, Foster stated "it is high time that a more definite understanding be reached between practicing physicians and investigators of the disease syndrome called mesenteric lymphadenitis." Our aim is to further this understanding. The forty-four cases analyzed in this paper were encountered in a small clinic, serving a community in which both the practicing physician and the laity are "appendix conscious."

Wilensky believes that mesenteric lymphadenitis is always secondary to another process in the body, usually infectious. It is important that this primary disease be discovered and remedied, as it is found frequently that only after removal of the primary focus will the pain cease. Otherwise, normal appendices will continue to be removed for "chronic appendicitis" and useless treatment continued for "post-appendectomy adhesions" when the true cause of the pain lies in the persistence of the enlarged nodes in the mesentery. It is obvious that until accurate differential methods can be described, operation must be carried out to exclude acute appendicitis. The removal of an appendix in which no pathological disturbance is present, however, does not relieve the surgeon of his obligation to continue his studies later in an attempt to find the real cause of the process.

The following classification based on the clinical picture is suggested by Rosenberg: (1) chronic mesenteric lymphadenitis, (2) acute mesenteric lymphadenitis, (3) acute fulminating mesenteric lymphadenitis, and (4) acute suppurative mesenteric lymphadenitis. Accordingly, our forty-four cases may be divided as follows: chronic seventeen, acute twenty-five, and acute fulminating two. We have had no cases of the suppurative type, but these have been reported by Tuberville, Borchard, Foster, Etchegorry, Porumbaru, Huggins, Segar and Rosenak, Schwyzer, and Wilensky and Hahn.

Occurrence. There are few reliable statistics available on the frequency of this condition. Struthers in two years had twenty-four cases of mesenteric lymphadenitis (including those of tuberculous origin) with 187 cases of appendicitis in the same period. Gage states that 60 per cent of his cases of chronic appendicitis showed mesenteric lymphadenitis. We consider our own statistics unreliable until January 1, 1941, because, prior to that time, we did not inspect carefully the mesentery of the terminal ileum in all cases of nonperforating appendicitis. Murphy, in 1908, mentioned enlargement of the mesenteric nodes in chronic appendicitis, while Noesske, in 1924, urged inspection of the mesentery in

cases with abdominal pain but an essentially normal appendix. As noted in the accompanying table, there has been a sharp rise in the number of cases in the past six months, and it is suggested that a diagnosis of mesenteric lymphadenitis would be made much more frequently if it were carefully looked for.

In this series of forty-four cases, there are twenty-six (59 per cent) males and eighteen (41 per cent) females. In 771 cases collected from the literature in which the sex was stated, there were 344 (44.6 per cent) males and 427 (55.4 per cent) females. The majority of reported cases are young, usually below thirty, and this was borne out in this group. The distribution by decades was: one to ten years, fourteen cases (31.8 per cent); eleven to twenty years, nineteen cases (43.1 per cent); twenty-one to thirty years, ten cases (22.7 per cent); and one patient was age thirty-two years.

By some authors, seasonal variation is thought to be of importance. The distribution of our cases is noted in Figure 1. Since only the first six months of this year have been included, it is obviously not a true representation. The distribution of our cases has thus far been fairly even throughout the year. We have noted, however, an increase in cases after any change regardless of season which favors infections, either respiratory or gastrointestinal, such as a sudden cold rain in mild weather or the first warm period suitable for swimming. It is difficult to evaluate these factors, but the impressions gained were very definite.

Etiology. Both Wilensky and Ireland have contributed excellent summaries on the possible causes of mesenteric lymphadenitis. The suggested agents range from a foreign body (Küper) to a virus (White and Collins). Many, including Brown Lamson, Speese, Coleman, Short, Segar and Rosenak, Powers, Porumbaru, Luzuy, and Ybarz believe the appendix is the site of the initial lesion. Wilensky and Hahn, Pribram, Bell and others have called attention to the analogous anatomic arrangements and relationships of the cervical lymph-nodes and lymphatic apparatus of the neck and the mesenteric lymph-

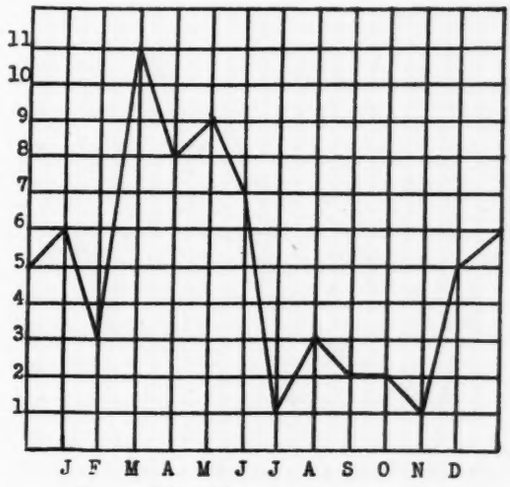

Fig. 1. Monthly rate of occurrence.

nodes and lymphatic apparatus of the intestine. Pribram has suggested that "the swallowing of lymphotropic bacteria from the tonsils may initiate inflammation of the appendiceal wall from where the mesenteric lymphatic system is then infected." It is doubtful if such an explanation is entirely or consistently true, but it serves as an excellent working basis, provided ileal wall be substituted for appendiceal wall in the statement. From the available evidence, it appears that the majority of cases are the result of the absorption from the lymphatic tissue of the ileum of bacteria, their toxins, or their decomposition products. The following case serves as an example:

W. H., a nineteen year old male, was first admitted because of a chronic draining sinus which followed a fracture of the left mandible. During the routine history, he mentioned that he had had frequent sore throats since the fracture occurred two months previously. Examination disclosed the tonsils to be enlarged and red. After satisfactory drainage of the osteomyelitis was established, he was discharged.

He returned two months later because of abdominal pain. The sore throats had continued, becoming more severe, and with each attack there had been abdominal pain. The present attack had started five days before;

the pain began and remained in the right lower quadrant, and was severe enough to confine him to bed. This, with the well localized tenderness, was considered sufficient to justify appendectomy. The appendix was grossly normal, but the lymph-nodes of the mesentery of the terminal ileum were enlarged and injected, the size varying from .1 to 1 cm. in diameter. The postoperative course was uneventful.

Following discharge, he continued to have exactly the same type of abdominal pain with recurrent tonsillitis. A month later the tonsils were removed. Streptococci, both hemolytic and nonhemolytic, were found in culture. Since the tonsillectomy, now a period of four months, abdominal pain has been completely relieved.

Further follow-up will be necessary, but it will only be by careful follow-up of all cases that the etiology of this symptom complex will be solved. A large group of cases, continuously observed, has not been reported.

History. Twelve of our patients had tonsillectomy and adenoidectomy from one to sixteen years prior to the onset of the disease. Seven patients gave histories of an acute upper respiratory infection shortly before or with the onset of the present illness. One patient, a fourteen-year old girl, had had slight leukorrhea since menarche two years before. Two patients gave a history of chronic otitis media, and the patient mentioned above had a chronic draining sinus from a low-grade osteomyelitis. Three patients described one similar attack of abdominal pain from one to two years before the attack requiring admission; three others had had several attacks during the year prior to the present illness; and four had been having recurring attacks for from two to six years. One patient had had an appendectomy six years before.

Twenty-six of the patients were seen within twenty-four hours of the onset of their illness and the remaining patients were seen within varying intervals up to two weeks. Pain was present in some stage of the disease in every patient; this was of varying intensity and location. In sixteen patients, the pain began and remained in the right lower quadrant. In the remaining patients, the pain at onset was as follows: in two, right upper quadrant; in seven, across the entire lower abdomen; in five, epigastric; in five, periumbilical; and in nine, generalized. Of these twenty-eight patients, the pain later localized in the right lower quadrant in nineteen. Further classification of the pain revealed that in five the pain was slight; in fourteen, moderate; in twelve, severe; and the history does not record the intensity in thirteen. Six patients described the pain as being colicky in nature; five as cramp-like; ten as aching; and two as sharp. In three cases, anorexia was a prominent complaint. In nineteen patients, there was vomiting, varying from one to ten times. Five additional patients complained of nausea without vomiting. Six patients had taken laxatives without relief and five had received enemas without relief. Eight patients gave a history of diarrhea, consisting of from two to eight watery stools, in one of which blood was described. Only two patients complained of constipation.

The symptoms are presented in detail to emphasize the difficulty of differentiation from appendicitis and other acute abdominal conditions. Various minor points of contention occur throughout the literature in reference to the history. For example, White states that diarrhea is rarely present and constipation the rule, while we find the opposite to be true. Foster finds the pain more apt to be steady, continuous and dull. Freeman, in his early paper, noted the colicky paroxysms of pain which "come and go without apparent cause" and regarded this as a valuable diagnostic symptom. Speese, Coleman, and Bell have attached significance to this paroxysmal type of pain. This has also impressed us. We find that while in acute appendicitis the pain is usually progressively more severe and in the majority of cases constant, that of mesenteric lymphadenitis is almost always subject to frequent exacerbations and remissions. A case illustrating this follows:

C. K., a fourteen-year old white girl, was admitted because of severe right lower quadrant pain. For the year before, occasional attacks had occurred. For seven days before admission, there had been one to three attacks daily of severe right lower quadrant pain with nausea and vomiting. The day of admission, an attack had occurred in the morning, with extremely severe colicky pain and vomiting, which was followed by two watery stools. The attacks usually lasted several hours and she felt fairly well in the intervals. On examination she appeared moderately ill. The face was flushed. The temperature was 100°F. and the pulse rate was 96. The tonsils were enlarged and red. There was moderate tenderness in the right lower quadrant, no spasm, and with tenderness on the right by rectal examination. The urine was negative except for one plus acetone; the leukocyte count was 17,400.

At operation, the appendix was grossly normal. The lymph-nodes in the mesentery of the terminal ileum were enlarged, varying from 0.5 to 1.5 cm. in diameter. They were injected and the overlying peritoneum appeared tense. The appendix was removed. Convalescence was uneventful.

The exact cause of the pain is problematic. Short believes it to be due to pulling on the mesentery during peristalsis. Speese and Rosenberg believe the cause to be the intestinal spasm. Brown feels the distention of the capsules of the nodes causes the pain. Freeman thinks it due to an irritation of the sympathetic filaments in the mesentery by the enlarged lymphatic nodes. We have found some correlation in the operative findings and the severity of the pain in that the greater pain is found in those cases which show a very tense peritoneum overlying the nodes, as if the node could be "popped out" with the slightest pressure. The patients with the chronic cases, however, when operated upon during an attack do not show this tenseness, but still have had the pain immediately before operation. For this reason, we cannot believe distention of the node capsule or overlying peritoneum can be the principal cause of the pain. It seems most probable that the pain is due to ileal spasm resulting either from absorption of bacteria or their products, or from disturbance of the sympathetic fibers which pass through the nodes, or to both.

Foster, Marshall, and Wilensky have noted the frequency of tonsillitis and other respiratory tract infections in mesenteric lymphadenitis. This has also been our experience. Both McFadden and Worley frequently find nausea and vomiting in their cases. It has been our impression that this is seen less often in mesenteric lymphadenitis than in acute appendicitis. This, however, seems to be of less differential value.

Examination. The temperature was below 102°F. in thirty-six cases; in seven from 102° to 104°F.; and in one case was 104.4°F. The pulse rate paralleled the temperature elevation. One case showed slight icterus, interpreted as catarrhal in origin. (One of Brown's cases also showed jaundice.) Three cases showed acute follicular tonsillitis. In twenty-eight cases, there was definite evidence of infection in the upper respiratory tract. Perforation of the drums with slight purulent drainage was noted in two cases. In one patient, there was a draining sinus of the left mandible. In two cases, the spleen was enlarged, both extending about 4 cm. below the left costal margin. Acute epidermophytosis of the feet was noted in two cases. In eleven cases, the cervical lymph-nodes were enlarged; in two, the epitrochlear nodes were enlarged; in two, the axillary; in one, the femoral; and in one case there was generalized lymphadenopathy.

From the above, it can be seen that in approximately 77 per cent of our cases, a focus of infection was found at the time of the first examination. McKechnie and Priestley found a focus of infection in 60 per cent of their cases; Emmett in 44 per cent; Ingegno in 43 per cent; and Foster in 57 per cent. Foster, Pribram, Parini, and Brennemann call attention to the greater frequency of upper respiratory tract infection in mesenteric lymphadenitis than in acute appendicitis. We regard as particu-

larly important that in so many cases an infection is found which could logically act as the primary focus. It is highly suggestive that further search would reveal a primary focus in nearly 100 per cent of the cases of mesenteric lymphadenitis. We have not separated those cases with acute upper respiratory infections from those with no obvious primary focus, as suggested by Wilensky, as we believe they should all be included in one group. The fact that in some the source is easily demonstrable, while in others it is found with difficulty does not seem sufficient reason for the differentiation. The important point to be emphasized is that the causative agent is absorbed from the ileum, and that the source of this agent should be discovered.

Bell has also reported a case with palpable spleen. Careful hematologic and immunologic studies in our two cases failed to reveal any cause other than the primary infection which we believe also brought about the mesenteric lymphadenitis. Both were young white men, age twenty-one and twenty-two. Foster and McFadden have also noted enlarged nodes elsewhere frequently.

Examination of the abdomen showed tenderness in forty-two of the forty-four cases. In twenty-nine, this was in the right lower quadrant and varied in intensity. Graded on the basis of one to four plus: in five, the tenderness was one plus; in seven, two plus; in seven, three plus, and in ten, four plus. Tenderness was maximal in the epigastrium in one case, at the umbilicus in one, and generalized in three. There was tenderness across the entire lower abdomen in eight cases. In seven cases, there was increased muscle tone, and in four, there was rebound tenderness. Two patients showed slight abdominal distention and one was markedly distended. On rectal examination, twenty of the forty-four showed tenderness on the right. In the latter half of the series, an attempt was made to elicit the shifting tenderness as described by Klein. This consists in placing the patient on the left side for thirty seconds or more, whereupon the tenderness, maximal in the right lower quadrant with the patient supine, shifts to the left lower quadrant. In only one of our cases of mesenteric lymphadenitis was this found. Curiously, two days after this patient was admitted, a twelve-year old white boy was seen with an acute upper respiratory infection, right lower quadrant pain, and tenderness which shifted with change in position. At operation, a gangrenous appendix was removed and no mesenteric lymphadenopathy noted. This is quoted merely to show that no definite pattern or sign occurs with dependable regularity in this condition.

We have noted with some frequency tenderness in the vicinity of McBurney's point extending to just above and to the left of the umbilicus. This is also mentioned by Gage, Ochsner and Murray, McFadden, and Schrager, and represents tenderness over the root of the mesentery. Freeman, McKechnie and Priestley, Ingegno, and Marshall have commented on the relative infrequency of spasm of the abdominal muscles, which has also been our experience. This is logical as the parietal peritoneum is rarely irritated in mesenteric lymphadenitis. Marshall and Foster have been able to palpate the enlarged mesenteric nodes in numerous cases. We have been unable to do this. McFadden describes an enlarged lateral sacral node on palpation by rectum. Mesenteric lymphadenitis is not to be confused with the acute iliac adenitis as described by Irwin.

In only twelve of our forty-four cases was mesenteric lymphadenitis made the primary diagnosis on admission. Thus in only 27 per cent of the cases was the original impression correct. Gross and Ladd state that mesenteric lympadenitis is the most common disease which must be differentiated from appendicitis in children. As experience with mesenteric lymphadenitis increases, the diagnostic errors become less frequent. In this series, appendicitis was diagnosed twenty-one times, usually being called acute in type. Salpingitis and

enteritis were diagnosed two times each, and the following conditions once: pyelitis, Meckel's diverticulitis, pylorospasm, cystitis, uterine retroversion, spastic colon, tubo-ovarian abscess, and torsion of pedunculated ovarian cyst. From the list of errors given above, it is apparent that the statement of Klein: "the diagnosis of mesenteric adenitis is not an elusive mystery, but is rather simple" has not been true in our experience. The following case serves as an example of the difficulty encountered:

A. Z., a twenty-two year old white woman, was admitted because of abdominal pain. Her family, marital and past histories were irrelevant. Fourteen hours before admission, she was awakened by severe colicky, generalized, abdominal pain. The pain was most severe just below the umbilicus. She had vomited all liquids taken and an enema had afforded no relief. The temperature on admission was 99.4°F., the pulse rate 68, and respirations 18. The only positive finding on examination was moderate generalized abdominal tenderness, most marked midway between the symphysis pubis and umbilicus. The urine was negative and the leukocyte count 16,800.

She was watched for six hours. The pain became even more severe, the tenderness increased and board-like rigidity of the lower part of the abdomen developed. Rectal examination showed tenderness on both sides. Despite the essentially normal temperature and pulse rate, operation was thought necessary. Several possibilities were considered, with perforation of a Meckel's diverticulum thought the most likely. At operation, the findings were entirely negative except for typical, large, tense lymph-nodes in the mesentery of the terminal ileum. Recovery was uneventful.

Accessory Clinical Data. The leukocyte count showed wide degrees of variation. The lowest count was 4,200 and the highest 55,800. An average of the 44 counts gave 15,600. There were thirteen counts below 10,000; eighteen between 10,000–20,000; and thirteen over 20,000. Hemoglobin determinations and red blood cell counts were done on all patients and were not unusual. Differential counts were recorded on twenty-eight patients. The majority showed a moderate polymorphonuclear leukocytosis; the highest being 93 per cent and the average 71 per cent. One case showed an eosinophilia of 10 per cent and in two other cases eosinophile counts of 4 per cent were noted. (One of Brown's cases had 6.5 per cent eosinophiles. Whether or not this tends to support the factor of allergy as an etiologic agent, as suggested by Ireland, is problematic.) Schilling hemograms showed a moderate tendency toward a shift to the left. Urine examinations were not unusual in all cases. Those who had vomited repeatedly had acetone, a few showed a trace of albumin, and a few white cells were found frequently on microscopic examination.

Oxyuris vermicularis were found by Ingegno in one case, by Ireland in one case, by Marshall in six, and by Heusser in several cases. In view of their findings, and because of occasional eosinophilia, from one to three stools were examined on twenty-four of our cases, and scrapings from the appendiceal mucosa were examined for parasites in ten others. All were negative and in no case were there signs or symptoms of this infection.

Sedimentation rates were done on twenty of the cases and varied from normal to 56 mm. per hour (Wintrobe). Kahn and Kline tests on eighteen of the patients were negative. From the work of Menefee and Poston, we realize that a single test does not rule out the possibility of Brucellosis. Nevertheless, macroscopic agglutination was carried out in twenty-four cases and all were negative. One of twenty-two patients subjected to intradermal test with 1:10,000 old tuberculin showed a positive reaction. In this single patient, a chest *x*-ray was negative and no calcified nodes found.

Heusser cultured colon bacilli in two of twenty-five cases. Adams and Olney found a hemolytic streptococcus in one node of two cultured. In culturing forty-eight nodes, Von Sassen obtained ten positives as follows: in five, Bacillus coli; in one, coli

and Bacterium aerogenes; in one, coli and hemolytic staphylococci; and in three, hemolytic staphylococci alone. Lawen, quoted by Von Sassen, found Bacillus coli in one case and hemolytic staphylococci in two others. Urech, in an unstated number of cases, cultured colon bacilli or enterococci from the nodes. Polichetti reports a diplococcus in a suppurative case. Goldberg and Nathanson cultured Streptococcus hemolyticus in one of eight cases. Gage has obtained an exceedingly high percentage of positive cultures. He reports finding an enterococcus in 93 per cent of sixty-five nodes cultured, either alone (67 per cent) or with the colon bacillus or a streptococcus. Marshall cultured Bacillus coli from nodes in two acute cases. Wilensky and Hahn found a Gram-negative bacillus in the abdominal fluid of one patient and recovered Streptococcus hemolyticus from the suppurative node of another. Lamson states that from the clinical course a streptococcus seems the most probable causative organism but offers no proof by culture. Kelly quoted an early case reported by Auguy in which Bacillus coli was cultured.

Lymph-nodes were removed and cultured aerobically and anaerobically in sixteen cases of this series. Positive cultures were obtained on two occasions. On the first, Bacillus coli was found. In the second case, the node selected for culture was a large one in the meso-appendix. A small Gram-negative diplococcus was found in both the aerobic and anaerobic cultures. This suggests two possibilities: Nodes near the appendix or bowel are more likely to yield positive cultures, and the appendix cannot be dismissed as the portal of entry, regardless of the anatomic evidence offered by Wilensky and by Klein.

The nodes of the mesentery are divided into three groups by Poirier and Cuneo: A primary group on the course of the terminal arterioles near the bowel, a second group at the level of the first anastomotic arch of the primary branches of the superior mesenteric artery, and a third group about the trunk of the superior mesenteric artery. The filtering action of lymph-nodes is well known, and it may be that the selection of a node in the primary group in preference to one in the second group will mean the difference between a positive and a negative culture.

Findings at Operation. The operative findings in this series were quite similar to those described in other communications. All patients were operated upon and the diagnosis of mesenteric lymphadenitis either confirmed or discovered. In six of the patients a slight excess of clear fluid was found on opening the peritoneum. In one case, slightly blood-tinged fluid was found and in one other, there was a large amount of grayish watery material present. The appendix was described as being grossly normal or at most slightly hyperemic in thirty-seven of the forty-four cases. In one case, the appendix had been removed previously. The remaining six cases showed acute inflammation of the appendix, two of which were frankly gangrenous. The terminal ileum and cecum felt and appeared normal in all cases except one. There was no evidence of lymphedema in the mesentery or bowel. The lymph-nodes in the mesentery of the terminal ileum were enlarged to a varying degree. In every case, it was noted that there was progressive enlargement of the nodes from the border of the intestine toward the root of the mesentery. Usually, at the mesenteric border the nodes were from 1 to 5 mm. in diameter, gradually increasing in size centrally to more than 2 cm. in size at the mesenteric root. The appearance of the nodes and the overlying peritoneum also varied and could not in all cases be correlated with the clinical findings. In the more acute cases the nodes appeared extremely tense and hyperemic, the peritoneum seemed stretched over them. In the subacute and chronic cases, the reaction appeared to be subsiding and the nodes presented a dull, purplish-red hue with no peritoneal reaction. Nodes were removed for culture and section in sixteen cases. This procedure was without

difficulty and in no case was the circulation of the bowel endangered. The appendix was removed in forty-three cases.

Ireland found mesenteric lymphadenitis in a patient who had had appendectomy nine months previously. Schnitzler reports a similar case with appendectomy eight years before. In Foster's series, four had prior appendectomies. In our case, the patient had had appendectomy six years before her admission here. She gave a history of recurrent attacks of abdominal pain over a period of two years. Operation was done to suspend a markedly retroverted uterus and mesenteric lymphadenitis found.

In three of our cases, calcified nodes were found in addition to the acutely involved nodes. In one of these, an abdominal *x*-ray was made seven months after operation and there was no evidence of calcification. He had experienced no further abdominal distress. The exact interpretation of this is difficult. The two others have been seen more than a year after operation and they, too, have had no more pain. Brown had one case with definite calcified nodes at operation; *x*-ray examination eight years later showed a faint vague shadow of questionable calcification. Kirkpatrick reports a case of intestinal obstruction caused by calcified mesenteric nodes. Short and McFadden, Colt and Clark discuss the severe pain which is frequently caused by calcified nodes. Auchincloss states calcified nodes may cause symptoms by forming adhesions or bands, by other nodes lesions of like nature, but active and not scarred or calcified, and by the presence of the nodes alone. Scheckter studied calcified nodes found on routine *x*-ray examinations in relation to clinical symptoms and concluded that they did not cause pain and tenderness as often as is commonly thought.

Wilensky states that the lymphatic drainage of the appendix is such that only a congenital abnormality will produce a mesenteric lymphadenitis secondary to acute appendicitis. Six of our patients had definite acute appendicitis, both grossly and on microscopic study. Two of these were gangrenous. Coleman reports that fourteen of his sixty-two cases, and Foster thirteen of his one hundred and fifteen cases had acute appendicitis and acute mesenteric lymphadenitis. Thus in 221 cases, 14.9 per cent had acute appendicitis, an incidence which seems considerably in excess of congenital abnormalities.

The acute fulminating type of mesenteric lymphadenitis is less frequently seen and the following case is one of the two which we placed in this classification:

K. R., a seven-year old white girl, was admitted because of severe abdominal pain. Her past history was negative except for a very severe upper respiratory infection one month before. For a week before admission, she had had a cold with moderate sore throat. Six hours previously, there had been the onset of extremely severe, colicky, abdominal pain, more marked in the lower part of the abdomen. There had been no nausea or vomiting, but anorexia was present. Her bowels were regular and no laxative had been administered. On examination, temperature was 102°F., pulse 130, and respirations 28. She appeared acutely ill, with flushing of the face and glassy eyes. The tonsils were markedly enlarged and red. The nasal mucosa was injected and there was a purulent nasal discharge. The heart and lungs were normal. The abdomen was moderately distended, with tenderness throughout, more marked in the lower part, and on the left greater than the right. There was spasm in both lower quadrants, which was marked, and also rebound tenderness. The femoral lymph-nodes were enlarged. On rectal examination, tenderness was present on the right. The urine was negative. The leukocyte count was 21,300 with 85 per cent polymorphonuclear forms.

On opening the peritoneum, there was an excess of slightly cloudy, sticky fluid. On smear, a Gram-positive coccus in clumps was found (later identified as Staphylococcus aureus). The entire peritoneum, with the appendix, cecum, and terminal ileum appeared hyperemic. The lymph-nodes in the mesentery of the terminal ileum were enlarged, firm and tense. The appendix was removed; no node was taken because of the positive smear. The abdomen was closed without drainage. Her postoperative course was uneventful. She

was given sulfathiazole 0.5 Gm. every four hours for forty-eight hours, and her temperature was normal on the third day after operation.

Wilensky has emphasized that "normals of size of lymph nodes have not been established and so fundamental diagnostic errors may occur." Mead concludes "visual differentiation is accurate, for the apparent size of a node is fairly indicative of its weight." We believe that in any case in which there are found a large number of lymph-nodes in the mesentery of the terminal ileum, measuring by estimation 0.5 cm. or more in diameter, pathologic enlargement may be assumed.

Pathology. Thirty-seven of the appendices removed showed no essential pathologic change. The remaining six presented the usual findings of acute appendicitis, with marked edema, polymorphonuclear leukocyte infiltration and areas of necrosis. The nodes removed showed only lymphoid hyperplasia with varying degrees of edema. There was no tubercle formation found.

Postoperative Course. In about 75 per cent of the patients, convalescence was uneventful following operation. The remaining patients had unusually trying courses; the main difficulties were abdominal distention and cramps which were extremely severe. Surprisingly, the degree of postoperative reaction could not be correlated with the severity of the illness before operation or the operative findings. Several of the patients with severe preoperative pain had little difficulty during convalescence, while two patients with chronic cases operated upon after the acute attack had subsided, had marked distress afterward. Further, most of the patients with cramps and distention responded well to the usual measures of clear liquid diet, hot packs, enema, and prostigmin, while a few were refractive to all therapy.

Usually, the temperature was normal by the third day, the patient out of bed on the fifth and home on the seventh. In two cases, there was an exacerbation of their upper respiratory infection. Five cases received one of the sulfonamides with perhaps some beneficial effect.

TABLE I

RATE OF OCCURRENCE AT THE PALMERTON HOSPITAL

Year	Appendectomies*				Mesenteric Lymphadenitis	Per Cent
	Acute	Recurrent	Incidental	Total		
1939....	96	42	45	183	3	1.6
1940....	90	44	43	177	20	10.1
First 6 mos. of 1941...	43	17	25	85	35	29.1

* Total appendectomies for period indicated; acute refers to appendectomy for acute suppurative, gangrenous, or perforated appendicitis; recurrent includes "chronic," subsiding, or interval cases; incidental appendectomies were done at other operations, usually gynecologic. This chart includes fourteen additional cases not included in the analysis of symptoms, etc.

No serious postoperative complications occurred in this series. Pribram had one death in which autopsy showed mesenteric lymphadenitis. Sobel and Stetten report one death of bronchopneumonia three days postoperatively. Adams and Olney had a patient who died five and one-half hours after operation; no definite cause was found. Ireland in twenty-two cases had one death due to peritonitis from rupture of a suppurative node (Streptococcus hemolyticus). McKechnie and Priestly also had one death in their series. Coleman reports that one of his patients, who had acute appendicitis and acute mesenteric lymphadenitis combined, developed peritonitis with paralytic ileus and expired. We have found no report of postmortem examination of the mucosa of the terminal ileum.

Follow-up. As indicated in Table II, of 371 reported cases followed, the various authors report cures in 67.9 per cent. These cures were after appendectomy and general hygienic measures. Marshall had cure of symptoms with improved general health "in a large proportion but admittedly not all" of his cases.

We have been able to recall and examine twenty of our forty-four cases after inter-

vals of from four to twenty-four months. Seventeen patients were completely well. Two patients had had gastrointestinal disturbances which were in no way similar to the symptoms preceding operation. One patient, a six-year old boy, was particularly interesting. He had continued to have pain in the right lower quadrant with each upper respiratory infection. Examination showed the tonsils to be markedly enlarged and chronically infected. Tonsillectomy was advised but has not as yet been carried out.

TABLE II
RESULTS OF FOLLOW-UP AFTER APPENDECTOMY

Author	No. of Cases Followed	Completely Well
Brown	30	30
Rosenberg	29	10
Adams and Olney	11	11
Sobel and Stetten	20	9
Gage	22	14
Wise	8	6
Klein	50	0
Ireland	20	16
Coleman	62	62
McKechnie and Priestley	49	36
Ingegno	30	25
Strömbeck	40	33
	371	252

SUMMARY

Nonspecific mesenteric lymphadenitis is a symptom complex which occurs much more frequently than is generally acknowledged. This assumes that the mesentery of the terminal ileum is inspected in all suspicious cases. The symptoms are found usually in children and young adults. Despite the statements of others, upper respiratory infections occur much more frequently in mesenteric lymphadenitis than in appendicitis. The etiology remains to be proved, but it appears to be secondary to infection elsewhere in the body, usually the gastrointestinal or respiratory tracts.

The factors most useful in differential diagnosis are the colicky recurring nature of the pain and the distribution of the tenderness over the root of the mesentery. The laboratory findings are of little aid. The leukocyte count varies markedly and cannot be correlated with the clinical findings. We cannot agree with those who consider that appendectomy alone cures the majority of these patients. We do agree, however, that operation is indicated because of the inability to exclude acute appendicitis in most cases.

CONCLUSIONS

1. Mesenteric lymphadenitis is a symptom complex of frequent occurrence which has not received due emphasis in texts and papers considering the causes of abdominal pain.

2. The node enlargement is always secondary, and in most cases, the primary source can be found and eradicated.

3. Operation with appendectomy is the treatment of choice unless more vigorous differentiation can be made.

4. Careful study and follow-up will lend much to the solution of the etiology, accurate diagnosis and proper treatment.

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Any operation on the breast which subjects the patient to radial or longitudinal incisions predisposes to more or less scarring. This should be avoided. Scars are constantly reminding the patient of the operation which she has undergone and, should there be a tendency to keloid formation, matters are much worse because of the effects produced by the keloid.

DIFFERENTIAL DIAGNOSIS AND TREATMENT OF ACUTE ABDOMINAL INJURIES*

METHOD EMPLOYED AT THE UNIVERSITY OF MINNESOTA HOSPITALS

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WITH the increasing number of automobile accidents in peace time and the frequency of bullet wounds to the abdomen in time of war, the problem of abdominal injuries becomes one of paramount importance. Most writers on this subject are concerned with the treatment and end results. However, both treatment and end result would be better if a more accurate diagnosis of the type of abdominal injury could be made.

In 1935, Wangensteen reviewed the general problem of abdominal injuries. He concluded that in all acute abdominal injuries, two factors influence the type of treatment to be given: First, whether the trauma was blunt or penetrating, and second, whether a hollow or solid organ was injured. It may be said that (1) nearly all injuries caused by penetrating trauma and certainly all injuries perforating hollow viscera should be operated upon as soon as the condition of the patient permits. (2) Injuries due to blunt trauma may or may not be operated upon, depending upon whether a hollow or solid viscus was injured. Subcutaneous injuries of the abdominal organs occur in the following order of frequency: Liver, spleen, kidney, intestine, stomach, bladder and pancreas (Greil). (3) Injuries to solid viscera such as liver, spleen or kidney are preferably treated conservatively as long as the blood pressure and pulse are stabilized and there is no marked fall in the hemoglobin and erythrocyte count.

Thus, the whole problem of the treatment of acute abdominal injuries resolves around this question: Given a history of trauma to the abdomen, how can one be certain whether a hollow or solid viscus has been injured? The purpose of this paper is to give a method of differential diagnosis of acute abdominal injuries employed on the Surgical Service of the University of Minnesota Hospitals, which has proved of distinct value.

ABDOMINAL INJURIES CAUSED BY BLUNT TRAUMA

In early cases of abdominal injury, the temperature, pulse, respiration, blood pressure, leucocyte count or degree of shock rarely give any information of value as to the location or degree of injury to the abdominal organs. The best indication of what organ has been injured is the location of the trauma.

Injuries to the omentum, mesentery and pancreas are impossible to diagnose with any degree of certainty. Fortunately, they do not occur very often. In reality, it is injury to the solid organs such as the liver, spleen and kidney and to the hollow viscera such as stomach, large and small intestine and bladder that is of diagnostic importance in abdominal injuries.

1. *Liver.* Injury to the liver may be suspected by the location of the trauma, the presence of liver tissue protruding from the wound, tenderness or abnormal dullness or percussion over the normal course of the ascending colon and elevation of the right diaphragm.

2. *Spleen.* When the spleen has been ruptured there is tenderness and abnormal dullness on percussion in the left upper quadrant; the dome of the left diaphragm may be elevated or there may be signs of a left pleural effusion. The hematoma may be

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felt on bimanual palpation. The ribs of the lower left chest are often fractures.

3. *Kidney.* Hematuria, pain in the back, a mass (hematoma) palpable in the flank should make one suspect renal injury. An *x*-ray of kidney, ureter and bladder and intravenous pyelogram may be diagnostic.

4. *Bladder.* In suspected rupture of the bladder the location of the trauma is helpful. As mentioned before, about half of these cases are associated with fractures of the pelvis. The patient will complain of hematuria, dysurea and oliguria or anuria. Failure to recover sterile saline injected into the bladder by catheter is not to be relied upon too strongly as a diagnostic sign of ruptured bladder. An important diagnostic measure is the cystogram taken not only in the anteroposterior and lateral views but also in the two oblique views. In making a cystogram it is better to inject a radiopaque substance, such as sodium iodide or diodrast rather than air (hoping to visualize the latter under the diaphragm by *x*-ray), as the chance of getting a negative result in rupture of the bladder is less when an opaque medium is used.

5. *Stomach and Large Bowel.* In injuries to the stomach and large bowel, where the viscus has been perforated, gas may be visualized under the diaphragm, especially on the right side. The history and location of the injury (compressed air forced into the rectum, impalement, foreign body in the rectum, etc.) will aid in the diagnosis of injury to the large bowel.

6. *Small Bowel.* When the small intestine has been rent by blunt trauma applied to the abdomen, the places that are the most likely to be involved are the two fixed portions: (a) near the ligament of Treitz and (b) near the ileocecal region. When the lower reaches of the small bowel are ruptured, gas is usually not visualized under the diaphragm by *x*-ray, due to the fine and intimate mixture of the gas with the food. In rupture of the retroperitoneal portion of the duodenum, the diagnosis may be made by the presence of gas around the kidneys by the roentgenogram. The diagnosis of rupture of the small bowel due to blunt trauma to the abdominal wall is the most difficult of visceral injuries to diagnose. Also it is surprising how indirect and relatively mild the trauma may be that causes rupture of the small intestine. One patient seen at this hospital had a tear in the terminal ileum after falling into a post hole and landing on her buttocks.

MANAGEMENT OF ACUTE ABDOMINAL INJURIES DUE TO BLUNT TRAUMA

When a patient who has suffered an acute abdominal injury due to blunt trauma is admitted in shock, it is imperative that the patient be brought out of shock before any diagnostic or therapeutic measures be directed to the abdominal injuries.

It is also a good rule to consider all patients in shock as though they had a head injury, fractured spine and abdominal injuries and *treat as such* until these possible injuries have been ruled out.

The diagnosis and treatment of patients with acute abdominal injuries due to blunt trauma are always easier if the patient is first seen two or three days after the injury than if they are seen immediately. As mentioned before, it is a tear in the small bowel that is most difficult to diagnose. Given a patient who has suffered blunt trauma to the abdomen, is not in shock and who on physical examination has pain, rigidity and tenderness of the abdomen, the diagnosis of injuries to the solid viscera will have to be made chiefly by the history, location of the trauma and the clinical signs discussed above. If a ruptured kidney is suspected, an *x*-ray of kidney, ureter and bladder and intravenous pyelogram are in order. If rupture of a solid organ is ruled out, an upright film of the abdomen should be made. If the roentgenogram fails to show free gas under the diaphragm, an open perforation in the stomach or colon is ruled out. If the rigidity, tenderness and even rebound tenderness are chiefly in the lower abdomen, a cystogram should be made to rule out a rupture of the bladder. If the cystogram is

negative, the patient should be explored, as there may be a tear in the small gut.

Some may say that a patient with an abdominal injury due to blunt trauma who shows signs of pain, tenderness and rigidity in the abdomen had best be operated upon. However, many patients with ruptured spleen, kidney and liver will be operated upon in such instances and it is known that most of these cases do well if not better under conservative therapy. The presence of gas under the diaphragm or extravasation of contrast media out of the bladder directs the surgeon's attention to the source of the peritoneal irritation. The upright film of the abdomen and cystogram are the best available methods of ruling out other lesions when considering perforation of the small gut. Unless procedures like peritoneoscopy come into more general use and give more accurate results, it is the only way that a differential diagnosis of a rupture of the small bowel can be made.

MANAGEMENT OF ACUTE ABDOMINAL INJURIES DUE TO PENETRATING TRAUMA

The introduction of the use of laparotomy for penetrating wounds of the abdomen, especially bullet wounds, was definitely an American contribution to surgery, although the first recovery from such an operation was reported by Kocher. In the period before the discovery of anesthetics and antiseptic methods, most surgical procedures were not only inadequate but were also doomed to failure because of subsequent shock and infection. Some surgeons, especially those with military experience, recognized that the ideal treatment consisted in opening the abdomen and repairing the injury. Many of the earlier surgeons, including Larrey, enlarged wounds due to firearms and repaired the damaged tissues, although they did not perform laparotomy in the modern sense.

A new era began with the advent of antiseptic surgery. Sims, in 1882, stated that laparotomy for bullet wounds was as feasible as that for ovariectomy. The end results of such laparotomies were and are far from comparable, however. Oberhelman and LeCount, in a review of the literature from 1893 to 1918 reported that of 1,494 patients with bullet wounds treated by laparotomy, 52.8 per cent died. Even up to World War I, there was some question as to whether a policy of non-interference, surgical interference in every case, or interference under certain conditions should be employed in the treatment of gunshot wounds. Amat enumerates twenty different meetings of the French society of surgery in Paris from 1886 to 1891 at which this subject was debated. At the meeting of the American Surgical Association in 1887, the members were asked to express their opinions as to whether laparotomy should be performed for penetrating gunshot wounds of the abdomen involving viscera.

The most convincing report on the value of an immediate operative attack as contrasted to conservative treatment of gunshot wounds of the abdomen is that of Enderlen and Sauerbruch. In 1915, they treated fifty-two cases of gunshot wounds to the abdomen conservatively and forty-six patients, or 94 per cent died. Of 211 patients with intestinal injury treated by laparotomy ninety-two, or 44 per cent, recovered. This improvement in the survival rate even under the adverse surgical conditions of war certainly proves the value of surgical treatment of gunshot wounds of the abdomen. In peace time a similar result was observed by Oberhelman and LeCount. Between the years 1911 and 1924 at Cook County Hospital, Chicago, there were 343 instances of bullet wounds to the abdomen. Of these 301 had laparotomies, of which 185 died (61.4 per cent). Of forty-two patients not operated upon, thirty-seven or 88 per cent died. It should be stated, however, that most of the patients in the latter group were in poor condition upon entrance into the hospital and died subsequently of shock. These authors also found that in wounds of single viscera the organs liable to be injured were as follows: Small intes-

tine, liver, colon and stomach. The mortality of injuries to the small bowel was 48.7 per cent. When there were injuries of two or more viscera due to bullet wounds, the mortality was 80.7 per cent, compared to that of 34.2 per cent for those with injury to a single viscus. They believed that the most important single element aiding the recovery of the patients with bullet wounds of the abdomen is a short interval between the injury and the operation. Also the experience of the surgeon in dealing with this type of injury is important. It is noteworthy that, in Oberhelman and LeCount's study, bullets entering the sides of the abdomen cause the most deaths; those entering the front are more often fatal than those entering the back.

TREATMENT OF ABDOMINAL INJURIES DUE TO PENETRATING TRAUMA

It is generally accepted that patients who die of bullet wounds to the abdomen within the first twenty-four hours after injury die from shock; when death occurs after twenty-four hours, it is usually due to peritonitis.

It is imperative that the patient with penetrating wounds of the abdomen be operated upon as soon as possible, but if the patient is in shock, he should be given blood transfusions or plasma until he is out of the shock level. Also, all patients with penetrating abdominal wounds, whether in shock or not, are potential candidates for shock and should be given blood transfusions during the operation as a safety measure. In our experience the type or length of anesthesia are not so important if the patient is given a transfusion during operation. Blood transfusions should be considered as much a part of the surgical procedure as the abdominal incision and the closing of the perforation.

In most instances it is enough just *to close* any perforation of the gut. Oberhelman and LeCount found that in only a few patients do the wounds require section of the viscera or parts of the viscera.

Postoperative drainage is a matter of opinion and depends somewhat upon the amount of peritoneal contamination at the time of operation. There are no convincing studies to prove that drainage has any advantage over tight closure of the abdomen in gunshot wounds. More important is the use of suction applied to an indwelling Wangensteen or Miller-Abbott tube to keep the bowel (a) empty, to prevent paralytic ileus and (b) quiet to allow localization of any peritoneal exudate.

Recently there is evidence to show that sulfanilamide is of value in preventing peritonitis in experimental animals (Jensen, Varco, Rea). Clinically, it is impossible to judge its value as yet (Ravdin). Experimentally, however, it has more protective value when used before peritonitis has developed than when peritonitis is already present. At present, sulfanilamide in doses of 3 Gm. is powdered into the peritoneal cavity at the end of operation where there has been gross or suspected contamination, and postoperatively the drug is given by mouth, 60 to 90 gr. a day, or subcutaneously in doses of 125 cc. of an 0.8 per cent solution every four hours. The blood level of the drugs as well as the hemoglobin, erythrocyte and leucocyte counts are checked daily and the dosage regulated accordingly. It should be mentioned also that there is an impression at the Clinic of the University of Minnesota Hospitals that sodium ricinoleate 1 per cent in doses of 3 to 4 ounces, poured into the peritoneal cavity is of value in preventing peritonitis, but experimentally it is not as effective in the pre-peritonitis stage as sulfanilamide (Rea).

Postoperatively, the two complications to fear after gunshot wounds of the abdomen are peritonitis and pneumonia. Whether the former develops depends very much upon the factors present at and before operation, as the length of time before surgery, type and number of wounds, organ involved, etc. However, the resistance of the patient may be bolstered by means of continued siphonage drainage to

an indwelling intestinal catheter, blood transfusions, judicious administration of para-oral fluids, sulfanilamide, etc. Pneumonia may be prevented to a large measure by intratracheal aspiration of bronchial secretions after operation and subsequently as often as may be necessary, by encouraging the patients to cough, breathe deeply and to change their position frequently. The use of chemotherapy, especially sulfathiazole and antisera, is invaluable if pneumonia develops.

SUMMARY

In all acute abdominal injuries, two factors influence the surgeon in his choice of a surgical or conservative way of treatment: (1) Whether the trauma was blunt or penetrating and (2) whether a solid or hollow organ was injured. It may be said that nearly all penetrating wounds and certainly all perforations of hollow viscera should be operated upon as soon as the condition of the patient permits. The question, however, is: Given a history of either blunt or penetrating trauma to the abdomen, how can one be sure as whether a hollow or solid organ has been injured? The history, location of the trauma and clinical findings are of prime importance, but patients who complain of abdominal pain, rigidity and tenderness should have an upright film taken of the abdomen to rule out the presence of free intraperitoneal gas. If no free gas is seen, an open perforation of the stomach and colon is ruled out. If the pain is in the lower quadrant of the abdomen, a cystogram should be made to rule out a tear in the bladder. If the cystogram and upright film of the abdomen are negative, and if the possibility of rupture of the liver, spleen and kidney are ruled out, the patient should be explored to rule out the possibility of a tear in the small bowel.

Injuries to solid viscus are best treated conservatively as long as the patient shows no signs of shock. While the mortality of penetrating wounds to the abdomen is about 50 per cent, the results following surgical treatment are far superior to those following non-interference.

The plan of pre- and postoperative care of such patients at the University of Minnesota Hospitals has been briefly outlined.

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A ROENTGENOGRAPHIC AID TO THE DIAGNOSIS OF LEFT SUBPHRENIC DISEASE

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THE diagnosis of left subphrenic disturbances has long perplexed the radiologist. Until quite recently it could be suggested only on secondary changes in the diaphragmatic and left basal lung shadows. Fixation and elevation of the left diaphragmatic dome, followed by pneumonitis and pleural effusion as the infection spread had been considered the most reliable available indication. Fluoroscopy of the chest for diaphragmatic mobility assumed special importance because the left diaphragm, which is normally freely movable, may be fixed but not necessarily elevated in the presence of subdiaphragmatic pathology.

In 1938, Anspach[1] indicated that separation of the fundus of the stomach from the diaphragm might be a radiologic finding suggestive of left subphrenic abscess. This would be noted if the stomach bubble were separated from the diaphragm, or the fundus could be visualized with barium, and was the first step toward a roentgenologic sign based on the anatomy of the left subdiaphragmatic space.

Soon thereafter Carter[2] specifically described the usefulness of determining the relationship between the left leaf of the diaphragm and the cardia of the stomach by examining the patient in the Trendelenburg position after a barium meal. This maneuver was successfully employed in three of the six patients he reported. Normally, the cardia of the stomach lies in close apposition to the diaphragm. He noted that an abscess in the left anterior subdiaphragmatic space displaced the stomach downward, medially and posteriorly, and one in the posterior space deviated the stomach anteriorly.

The object of this article is to stress that separation of the cardiac end of the stomach and/or the splenic flexure from the diaphragm is a definite radiographic sign in the diagnosing of left subdiaphragmatic pathological conditions.

According to Ochsner and Graves,[3] the left subdiaphragmatic space is divided into three compartments. The *left anterior intraperitoneal space* is bounded by the diaphragm above, adhesions between the stomach or omentum to the anterior abdominal wall below, the left lobe of the liver to the right and below, the spleen to the left, the coronary and falciform ligaments to the right and the left lateral ligament behind. This space is most frequently affected. Abscesses may be localized to smaller areas created by adhesions within the space. It can readily be seen how the relatively yielding upper anterior wall of the stomach might be displaced by a collection between it and the diaphragm.

The *left posterior intraperitoneal space* is the lesser peritoneal sac. This space might be involved by perforation of a gastric ulcer or posterior wall gastric carcinoma.

The *left extraperitoneal space* is the loose areolar tissue which surrounds the kidney, pancreas and descending colon on its posteromesial aspect. Abscesses in this area may follow an infection of the vertebral bodies, a long standing chronic empyema, a perinephric abscess or a perforation of an adherent gastric ulcer posteriorly.

Left subphrenic abscesses occur about one-third as often as on the right. Their diagnosis is difficult, one of the chief reasons being that it is usually overlooked as a possibility in the differential diagnosis. However, not all subphrenic collections are

due to infection. Of the three cases reported here only one was an abscess. The second was caused by a large perforating neoplasm

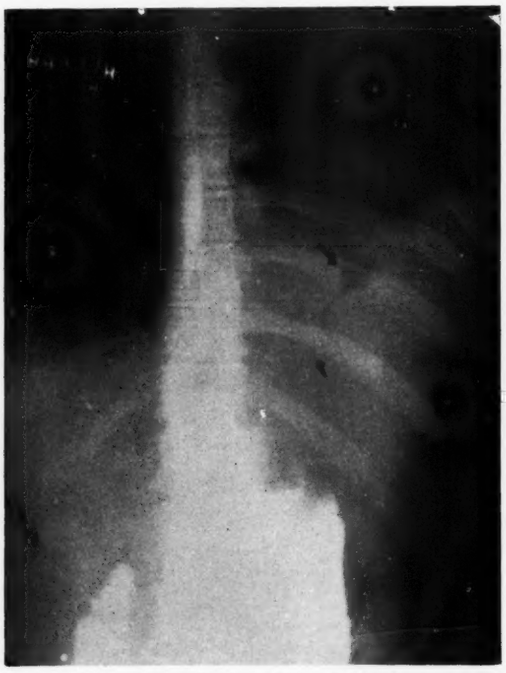


Fig. 1. Pronounced elevation of diaphragm and mesial displacement of cardiac end of stomach resulting from carcinomatous deposit in the left subdiaphragmatic space secondary to carcinoma of cardia. Note free air in tumor from perforation of necrotic gastric neoplasm. Study made with patient in Trendelenburg position.

of the cardia and the third by a nonspecific granuloma secondary to a minute perforation in the splenic flexure. In the first two cases the diagnosis was established by the separation of the cardia from the diaphragm, and in the third the splenic flexure was definitely depressed.

CASE REPORTS

Case 1. I. S., a thirty-five-year old man had complained of persistent, dull backache and vague abdominal discomfort for two years. One episode of acute pain had been diagnosed as appendicitis eighteen months before. Appendectomy was performed but no relief of pain followed. Three weeks before admission he first noted tarry stools. Four days before admission there was a large hematemesis with loss of consciousness.

When admitted he was pale but well nourished. His abdomen was tympanitic and there was slight spasm in the left lower quadrant. A mass which was considered to be an enlarged spleen was felt in the left hypochondrium. The breath sounds at the left base were diminished. His liver was palpable 5 cm. below the costal arch.

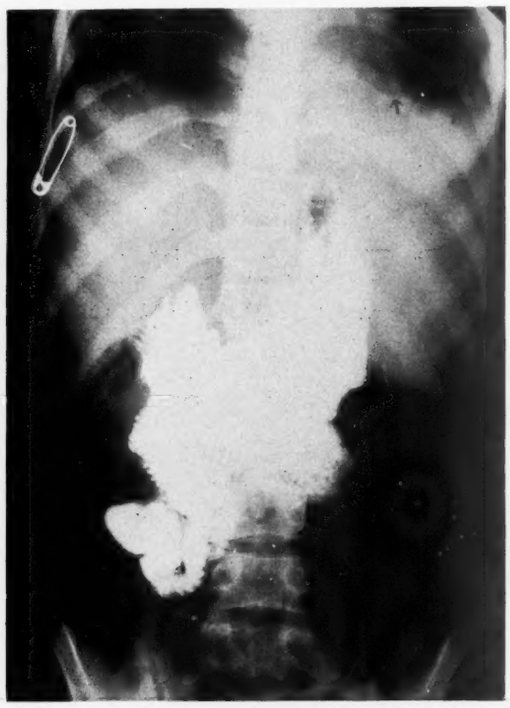


Fig. 2. Increased opacity of the left subdiaphragmatic area with narrowing and displacement of the cardiac end of the stomach downward and mesially by a subdiaphragmatic abscess. Note the distance between the left diaphragmatic cusp and the upper end of the cardia. Film taken with patient in prone position.

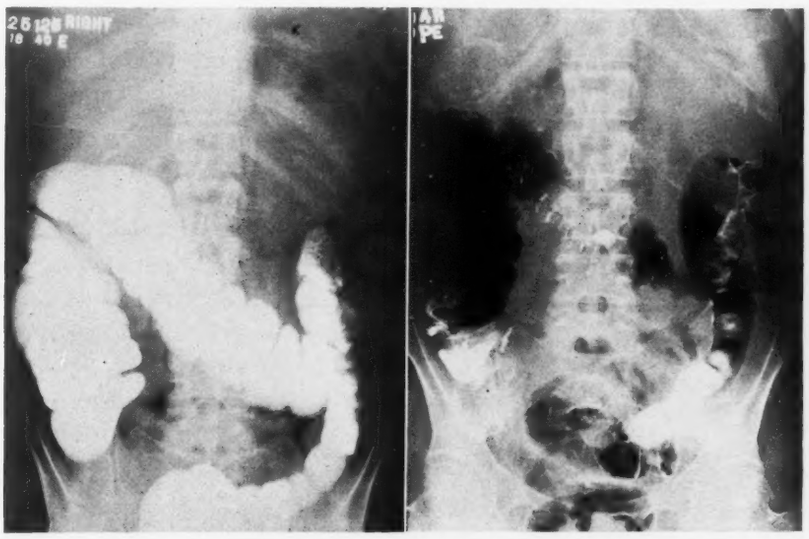
Radiographic examination of the chest showed a moderate pleural effusion at the left base. Films taken with the patient in the Trendelenburg position after a barium meal showed a pronounced separation of the diaphragm from the cardiac end of the stomach. At first this was considered to be due to pressure from the supposedly enlarged spleen. The possibility of a large neoplasm at the cardiac end of the stomach was suggested in the *x*-ray report.

His course was progressively downhill. A clinical diagnosis of hepatosplenomegaly of unknown etiology was made.

At autopsy there was a tremendous carcinoma arising from the cardia. A large mass of neoplastic tissue separating the stomach from the diaphragm was present. It extended

through the left leaf into the lung. On cut section the mass was found to be necrotic and contained a small amount of air. (Fig. 1.)

abdomen. The patient was given a barium meal and a definite separation of the cardiac end of the stomach from the diaphragm was demon-



A B

FIG. 3. A, the distal loop of the splenic flexure is depressed by a suprajacent granulomatous mass which fills the subdiaphragmatic space. Note distance between the diaphragm, indicated by arrows, and the splenic flexure. B, barium-air contrast study showing depressed splenic flexure and narrowed lumen of infiltrated distal loop.

CASE II. E. H., a sixteen-year old girl had bilateral peritonsillar abscesses during June, 1940. She made an uneventful recovery following incision and drainage. Three months later she was readmitted suffering from severe epigastric and left upper quadrant pain which was attributed to a blow in the left upper abdomen about a week before admission.

The spleen was not palpable when first examined. One week later it was enlarged 2 cm. below the costal margin. Her temperature ranged between 100° and 105°F. accompanied by severe chills. Exquisite tenderness over the upper portion of the abdomen with distention was present. The following week a tender, tense mass was palpated in the left upper quadrant. There was no abdominal rigidity.

Radiographic examination of the chest was normal on admission. Two weeks later a slight haze appeared at the left costophrenic sinus, but the diaphragmatic mobility was unimpeded. The opacity at the left base increased until a well defined pneumonitis and pleural effusion developed. In view of the clinical course and radiographic findings a diagnosis of a left subphrenic pathological disorder was ventured. Soon thereafter an opacity in the left upper quadrant was noted on direct *x*-ray study of the strated. A diagnosis of left subdiaphragmatic collection was made.

Subsequently 4 cc. of bloody purulent material was aspirated from the left subdiaphragmatic space. At operation the twelfth left rib was resected revealing a large granulating mass in the subphrenic space within which was an abscess. It was believed to be metastatic from the peritonsillar infection. The patient made an uneventful recovery. (Fig. 2.)

CASE III. I. R., a forty-five year old woman had complained of sharp pain in the left lower quadrant radiating to the back four months previous to admission. This disappeared and was followed by a constant dull ache. Two weeks before admission the pain recurred. There was loss of appetite and occasional vomiting. One week later she suddenly became constipated, had intermittent abdominal cramps and evacuated dark red blood clots. She lost fifteen pounds in four months.

Examination revealed a smooth, round, slightly tender, ballotable mass in the left upper quadrant extending 1 cm. below the level of the umbilicus. The liver was palpated 2 cm. below the costal margin. A clinical diagnosis of neoplasm of the kidney or splenic flexure was made.

A retrograde pyelogram showed the left kidney to be normal. A barium enema revealed the splenic flexure to be depressed below the horizontal level of the hepatic flexure. There was a constant filling defect 6 cm. long in the distal loop of the splenic flexure, irregularly narrowing its lumen. The findings were interpreted as indicative of an intrinsic lesion of the bowel, either neoplastic or inflammatory, with possible perforation resulting in a retroperitoneal mass which displaced the splenic flexure downward.

At operation the tumor in the left upper quadrant was found to consist of splenic flexure and an extrinsic mass which extended therefrom toward and involving the transverse colon. It also extended retroperitoneally to the right of the midline. At the junction of the splenic flexure and descending colon, corresponding to the site of the filling defect on the radiogram, the bowel was thickened, friable and inflamed. A Rankin obstructive resection was performed. The pathologic diagnosis was "colon with colitis and nonspecific granulomatous pericolitis." The patient made a good recovery. (Figs. 3A and B.)

COMMENT

Visualization of the stomach with barium, followed by examination with the patient in the Trendelenburg position, normally demonstrates close apposition between the cardia and the diaphragm. In the presence of a left subdiaphragmatic pathological condition, separation of these two structures can be demonstrated radiographically. Similarly, depression of the splenic flexure may be indicative of left subphrenic disorders, inasmuch as it normally rests close to the left diaphragm and at a higher level than the hepatic.

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GAS BACILLUS INFECTIONS COMPLICATING SURGERY OF THE UPPER URINARY TRACT

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INFECTIONS with the gas bacillus are far from uncommon, particularly in traumatic surgical practice and in surgical procedures carried out upon the gastrointestinal tract. The incidence of this infection occurring as a complication in urologic surgery is much less, and it is particularly small in surgery confined to the upper urinary tract, there being but twenty-four definitely recorded cases including the one about to be described.

ETIOLOGY

So-called "gas-bacillus" infections may be due to a variety of bacteria. The predominating organism, however, is the Bacillus welchii, designated also as Clostridium welchii bacillus aerogenes capsulatus. This organism was first described by Welch and Nuttall in 1892. Bacillus welchii is also known as Bacillus phlegmones emphysematose (Fraenkel) and as Bacillus perfringens (Veillon and Zuber). Next in frequency to Bacillus welchii is the Vibrion septique of Pasteur, and finally the Bacillus edematiens of Weinberg and Sequin and the Bacillus hystolyticus.

THE ORGANISM AND ITS MODE OF DETECTION

Bacillus welchii appears on the stained smear as a large, thick, gram-positive, rod-shaped bacillus. Smears taken from an infected wound may be positive as soon as six hours after the onset of infection, while cultures may be positive within four hours. On the serum agar plate the superficial colony appears moist and circular with clear cut edges. Stabs made in freshly boiled litmus milk will reveal the growth in twelve to fifteen hours, the milk becoming partially coagulated and giving off an odor of butyric acid. To be effective, media must be fresh and prepared under strict anaerobic standards. The most reliable diagnostic test for this organism is the test introduced by Welch and Nuttall, in which inoculations are made in rabbits. In this test, the animal's blood acts as the culture medium. Rarely do blood cultures become positive, which might be due to the inhibiting influence of the oxygen present in the blood stream.

Bacillus welchii has been found in feces, garden soil, dung, room sweepings, glass syringes and in a variety of other sources. It is normally present in the gastrointestinal tract of man and animals without producing gas. These same organisms, however, under abnormal environmental conditions such as intestinal perforation, gangrenous appendicitis or intestinal obstruction may and frequently do take on gas-producing propensities. Cases have been reported in which the Bacillus welchii was found in surgically extirpated gallbladders, the apparently normal vagina, and in wounds presenting no clinical evidence of infection (Kraft, Aschoff). Bacillus welchii has also been found present for long intervals outside the gastrointestinal tract without producing gas. In fact, Hendry reported two cases of Bacillus welchii infection in which symptoms appeared ten years after the injury occurred, indicating that under certain conditions, such as trauma or surgery, organisms originally possessing a low grade of virulence may

become activated and lead to fulminating sepsis.

PATHOLOGY

For Bacillus welchii to take root and flourish in a wound, the two prerequisites are a complete absence of oxygen and the presence of devitalized tissue. Both of these conditions are satisfied in a variety of wounds, such as crushing wounds, punctured wounds, lacerations associated with severe injury to adjoining structures, wounds harboring foreign bodies and particularly those carried in from the outside. The usual period of incubation is from one to six days, the average being three days, although infections may appear a few hours after injury or as long as ten years after injury. Structures possessing a good blood supply are less apt to become infected than when the blood supply is limited, as is illustrated by the infrequency of Bacillus welchii infections in head and neck injuries. Bacillus welchii infections show a marked predilection to spread rapidly along muscle bundles, although they may spread in connective tissue planes and along subcutaneous spaces.

As a rule, this type of infection rarely gives rise to frank pus unless it is complicated by pyogenic organisms. The discharge is serosanguineous in character and presents a characteristic sweetish, mousy odor which, once smelled, is rarely forgotten. The presence of gas bubbles in the tissues is one of the diagnostic features of this infection. Death is due to toxemia rather than to blood invasion, the toxins involved being primarily those resulting from the organisms rather than from tissue degeneration.

SYMPTOMS AND DIAGNOSIS

The disease is usually ushered in by an abrupt rise in temperature and by an increase in the pulse rate, the latter being out of all proportion to the elevation in temperature. The respiratory rate is also increased, which may erroneously lead to the suspicion of a pulmonary complication. Soon after the rise in temperature, the patient complains of pain in and around the region of the wound. Early inspection of such a wound will disclose swelling, with a more or less normal appearance of the skin surrounding the wound edges. Shortly thereafter the skin becomes pale and tense and presents a slightly yellowish tint. Purplish patches frequently follow the yellowish discoloration. These grow larger, frequently coalesce and form blebs containing a serosanguineous fluid with a characteristic sweetish, mousy odor. At a still later stage the purplish color changes to a dirty green. Occasionally, the affected part presents a bronze hue. Palpation reveals a sense of distinct crepitation extending from the wound to the outlying regions of integument. The presence of air in the tissues may be disclosed much sooner by *x*-ray than by the palpating hand. Positive cultures and smears made from the wound clinch the diagnosis.

TREATMENT

As soon as the diagnosis is made, or, better still, suspected, the wound should be laid wide open. The entire involved region should also be exposed by liberal incisions. Muscle planes should be bluntly separated rather than divided. Frequent copious washings with oxygenized antiseptics such as hydrogen peroxide or freshly prepared Dakin solution must be instituted. Seratherapy is highly desirable in this type of treatment and should be started as soon as the organism is found, employing preferably a mixed or polyvalent perfringens serum administered locally, subcutaneously and intravenously. The product commonly employed is the one containing 10,000 units of Vibrion septique antitoxin in each syringe package. The patient's sensitivity to serum must be ascertained before employing the serum intravenously. *X*-ray therapy has been employed with good results in early cases.

ANALYSIS OF TWENTY-FOUR CASES OF GAS BACILLUS INFECTION FOLLOWING SURGERY OF THE UPPER URINARY TRACT

Sex. In five of the twenty-four patients the sex was not stated. Of the remaining nineteen patients, thirteen (68.4 per cent) were males.

Age. Of the nineteen patients whose ages were noted in the protocols, there were none listed in the first and second decades, nor after the sixth decade. In the third decade there were five patients, four in the fourth, and five in the fifth and sixth.

Side Involved. The side involved was noted in eighteen instances, and of these, the left side was involved in ten patients (56 per cent).

Organs Involved. In the total series of twenty-four cases, the kidney was involved in twenty-two patients (91.7 per cent) and the ureter in two (8.3 per cent).

Preoperative Diagnosis. There were fourteen operations performed for calculi (58.3 per cent), twelve upon the kidney and two upon the ureter; and in five of these fourteen cases the condition was associated with pyonephrosis. In eleven instances (45.8 per cent) the kidney was the seat of infection, and in five of these the infection was associated with calculi. Three patients were operated upon for tumor (12.5 per cent), two of which were malignant and one benign (renal cysts). The group presents but one instance of hydronephrosis apparently without stone or infection. This was in a patient with a horseshoe kidney (Rathbun), in which one side was hydronephrotic and in which a heminephrectomy was performed.

Types of Operations Performed (Twenty-one Cases)—(in Three the Procedure Was Not Stated). Bacillus welchii infection occurred in ten patients following nephrectomy (47.6 per cent), in four instances (19 per cent) following nephrotomy, in four (19 per cent) following pyelotomy, and in two (9.5 per cent) following ureterolithotomy. The simple removal of two cysts from one kidney was followed by this type of infection in one patient (Mencher and Leiter). It might be mentioned that in this patient a suprapubic cystotomy for hypertrophy of the prostate was also performed at the time of the renal operation.

Treatment and End Results. The end results were tabulated in twenty cases, and it is from this group that statistics are computed. There were fourteen patients (70 per cent) who recovered, and six (30 per cent) who died. Of the fourteen patients who recovered, there were ten (71.4 per cent) who received serum along with the routine local treatment, and four (28.6 per cent) who did not. In the group of six patients who succumbed, two died before any treatment could be given, leaving four who died in spite of treatment. These four patients received routine treatment along with polyvalent perfringens serum.

CASE REPORT

G. C., male, aged fifty-six, a leather goods worker, complained of left lumbar pain of two years' duration. Save for a bilateral herniaplasty performed fifteen years previously, the past history was entirely irrelevant.

Physical examination revealed a well developed, highly nervous man, fifty-six years of age, who did not appear acutely ill. The two outstanding features of the examination were left costovertebral tenderness and a large boggy prostate. The urine showed a faint trace of albumin and twenty to thirty white blood cells per high power field.

Hemoglobin was 13.4 Gm. per 100 cc. of blood. The Wassermann test was negative.

Cystoscopy, which was performed elsewhere, disclosed a few red blood cells and leukocytes from the left renal specimen. Cultures were sterile.

A flat film of the genitourinary tract disclosed a large calculus about the size of a peanut kernel situated in the lower calyx of the left kidney, and a smaller calculus about the size of a split pea situated in the region of the upper calyx. The left renal silhouette was enlarged.

Under spinal anesthesia the left kidney was exposed through an eight-inch Albarran incision. The organ was enlarged to about one and

a half times the size of normal, and presented a considerable degree of perinephritis. Situated in a dilated lower calyx there was a large fragmented stone aggregating the size of a large peanut kernel.

The kidney was freed from its adhesions, delivered into the wound, carefully surrounded with moist pads, and through a small incision made through the parenchyma just above the lower pole, one of the calculi was palpated and removed in fragments. The calculus in the upper calyx was removed with difficulty through a small incision made through the renal parenchyma just below the upper pole, and supplemented with a small counter incision on the anterior surface of the kidney after fixing the calculus with the tip of the index finger introduced through the larger opening. All wounds were closed with mattress sutures of heavy plain catgut incorporated over pieces of muscle tissue. Over each incision a strip of fat was lightly anchored into place. At no time during the procedure was there any question of entering the peritoneum or of injuring the colon. The wound was closed in layers after draining the renal fossa with one rubber tube and a piece of rubber dam. There was very little loss of blood during the entire operative procedure, and he was returned to his room in excellent condition.

Approximately seven hours after operation the temperature rose to 102°F., the blood pressure dropped to 80/60, the pulse became thready and of poor quality, and the facies assumed an anxious expression. Although he presented many of the features of shock, his skin remained warm. Intravenous drip infusion of glucose and saline was immediately started along with the routine treatment for shock. The following morning he was given 500 cc. of citrated blood, but this failed to produce any appreciable improvement in his general condition. That night the blood pressure was 100/80. Forty-eight hours after operation the temperature rose to 103.4°F., and his skin became slightly icteric, and the pulse imperceptible. Examination of the wound disclosed an enormous edema; and the surrounding skin showed a purplish discoloration extending up to the level of the scapula. There was no evidence of crepitation at this time. The superficial layer of the wound was promptly laid open and a slight amount of seropurulent exudate was evacuated. Tubes were introduced for dakinization. The next morning he appeared septic, and distinct crepitation around the wound was elicited. There was a sweetish, mousy odor to the discharge. Smears and cultures showed the presence of Bacillus welchii.

Under cyclopropane anesthesia, all layers of the lumbar wound were laid wide open, and long incisions made in the chest wall. Muscle bundles were freely separated as far as the scapula. Free gas bubbles could be seen in the exposed tissues. The wound was inundated with hydrogen perioxide and 12 Gm. of sulfanilamide crystals were placed into the tissues. Polyvalent perfringens serum was administered subcutaneously and intravenously, and oxygen given through a BLB* mask. Although the temperature dropped to 100°F., the patient succumbed the following morning from sepsis. A postmortem examination could not be obtained.

Comment. Immediately following the diagnosis of Bacillus welchii infection, the bacteriological department made a thorough investigation of all catgut and supplies of the operating room with negative results. No cases of Bacillus welchii infection had been seen at this hospital in the past several years. Operations performed subsequently were also uncomplicated, indicating thereby that the infection could not possibly have been contracted in the operating room.

Since it is certain that the intestine was not injured during the course of the nephrolithotomy, this source can definitely be ruled out as playing any role in this case.

In view of the fact that we were dealing here with a patient with a fragmented calculus, it is quite possible that the calculus harbored the Bacillus welchii organism, as was evident in the case presented by Ferrier and Bliss, in which bacilli were found in the center of the calculus. Yet, Mencher and Leiter noted the fact that routine bacteriological examinations of renal calculi disclosed three instances of stones which harbored Bacillus welchii, but in none of these three patients did the wound become infected. Unfortunately, no bacteriological examination was carried out upon the calculi in this case.

* Boothby, Lovelace Bulbulian.

SUMMARY AND CONCLUSIONS

Gas bacillus infections complicating surgery of the upper urinary tract are rare, there being but twenty-four definite cases collected from the literature, including the case here presented. Although gas bacillus infections may be due to a variety of organisms, the predominating one is the Bacillus welchii. This organism has been found in tissues recovered from patients who presented no clinical evidence of wound or systemic infections. It has also been found in four renal calculi, but in only one of these was it associated with wound infection. In this instance the stone was fragmented during its removal.

While the usual incubation period varies from one to six days, the average being three days, it has been known to be as soon

TABLE I

Author	Sex	Age	Side	Diagnosis	Operative Treatment	Treatment of Infection	End Result
Howald, R.	Female	34	Left	Tuberculous pyonephrosis	Nephrectomy	H_2O_2 plus serum	Recovery
Meyer, A. W.	Male	54	Left	Calculus pyonephrosis	Nephrectomy	H_2O_2	Recovery
Idem	Female	66	Left	Calculus pyonephrosis	Pyelotomy	H_2O_2	Recovery
Idem	?	?	?	Stone	Pyelotomy	H_2O_2	Recovery
Idem	?	?	?	Stone	Pyelotomy	H_2O_2	Recovery
Turner, B. W.	Male	36	Left	Stone	Nephrolithotomy	H_2O_2 plus serum	Died
Idem	Female	30	Left	Stone plus cortical abscesses	Nephrectomy	Dakin plus *x*-ray Rx	Died
Weintrob and Messeloff	?	?	?	Sarcoma of kidney	?	?	?
Doering, H.	?	?	?	Pyonephrosis (pus in kidney showed Bacillus welchii)	?	?	?
Idem	?	?	?	Perinephritic abscess	?	?	?
Ferrier and Bliss	Female	40	Left	Stone	Pyelolithotomy	Dakin plus serum	Recovery
Knapper, C.	Male	30	?	Calculus pyonephrosis	Nephrectomy	No treatment	Died
Rathbun, N. P.	Male	26	Left	Hydronephrosis in horseshoe kidney	Heminephrectomy	Dakin plus serum	Recovery
Lowsley and Hunt	Male	46	Left	Stone	Nephrotomy	H_2O_2 plus serum	Died
Mencher and Leiter	Male	60	Left	Carcinoma	Nephrectomy	H_2O_2 plus serum	Recovery
Idem	Male	60	Right	Stone	Pyelonephrolithotomy	H_2O_2 plus serum	Recovery
Idem	Male	36	Right	Tuberculosis and left epididymitis	Nephroureterectomy and left orchidectomy	H_2O_2 plus serum	Recovery
Idem	Male	22	Right	Tuberculosis	Nephrectomy	H_2O_2 plus serum	Recovery
Idem	Female	42	Right	Calculus pyonephrosis	Nephrectomy	H_2O_2 plus serum	Recovery
Idem	Male	50	Right	Cysts of kidney and hypertrophy prostate	Removal of cysts and suprapubic cystotomy	H_2O_2 plus serum	Recovery
Idem	Male	50	Right	Tuberculosis	Nephrectomy	Oxygen plus dakin plus serum	Died
Idem	Male	24	?	Stone in ureter	Pelvic ureterolithotomy	H_2O_2 plus serum	Recovery
Idem	Female	44	Right	Stone in ureter	Ureterolithotomy	None	Died
Lazarus, J. A.	Male	56	Left	Stones	Nephrolithotomy	H_2O_2 plus serum plus sulfanilamide plus oxygen	Died

as a few hours after operation, and as long as ten years after inoculation. The outstanding clinical features of this infection are a rise in temperature and pulse rate, marked toxemia, edema and pain in the wound which presents typical purplish discoloration of the surrounding skin, followed later by coalescing blebs. The diagnostic features are crepitation in the subcutaneous tissues, a typical sweetish, mousy odor to the serosanguineous discharge, and positive smears and cultures of Bacillus welchii. Smears may be positive within six hours, and cultures four hours after the onset of infection.

Treatment consists of wide open drainage, generous use of oxygenized antiseptic solutions, along with polyvalent perfringens serum. It is quite possible that sulfonamides administered locally and orally may play a great rôle in the future handling of this type of infection. In early cases deep *x*-ray treatment has given gratifying results. In the collected group, 70 per cent recovered, and of this number, 71.4 per cent received serum. In the group of six patients who succumbed, two died before any treatment could be given, and the remaining four had received serum.

In the entire series of twenty-four cases, the kidney was the source of infection in twenty-two patients (91.7 per cent) and the ureter only twice (8.3 per cent). In 47.6 per cent of the cases the operations preceding the infection were nephrectomies; in 19 per cent nephrotomies; and in 19 per cent pyelotomies. Calculi were present in fourteen patients (58.3 per cent), twelve renal and two ureteral. And in five of these fourteen patients a co-existing pyonephrosis was present. Renal infections necessitating nephrectomies were present in eleven instances (45.8 per cent) and in five cases the infection was associated with calculi.

A case is presented, in which a fulminating Bacillus welchii infection followed nephrolithotomy for calculi, one of which was fragmented. Clinical evidence of infection appeared seven hours after operation.

Although W. M. Miller collected 607 cases of gas bacillus infection, there were only six which followed operations upon the genitourinary tract. In view of the fact that the type of operation was not mentioned, and no other details available, these six cases are omitted from the series. It is possible that Miller might have included some of the above tabulated cases in his collection.

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THE MENSTRUAL CYCLE IN THE HUMAN CERVICAL MUCOSA AND ITS CLINICAL SIGNIFICANCE*

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SIX years ago a systematic histological study of the human cervical mucosa in the intermenstrual period was begun, and observations have been reported in several previous communications.[1,2,3] Characteristic cyclic changes were found in the columnar epithelial elements. These cells cover the endocervix and line the glands. In the early proliferative phase the columnar cells are low, contain little cytoplasm, and they have sharply outlined, regular contours. The nuclei in this menstrual phase are small, deeply stained and are regularly arranged close to the basal membrane. An active proliferation can be observed in this cell type during the intermenstrual period. There is an increase in the number of the cells, they become gradually higher and broader, the cytoplasm increases, the nuclei become larger and elongated, some of them assuming a spindle shape. The nuclei also change their position within the cells, migrating toward the center. At the end of the proliferative phase, signs of accumulating secretion are seen in the cells. In the secretory phase the outline of the individual cells becomes irregular, they are bulging on their surface, and many of them are seen secreting. The nuclei are pale, spindle shaped and densely crowded. Immediately before, or at the beginning of menstruation the columnar cells become exfoliated, which process is rapidly followed by regeneration. The re-epithelization of the surface begins from the base of the glands from where the lining epithelium grows over the denuded surface. The columnar cells covering the surface and those lining the glands take equal part in the cyclic transformation.

Due to the proliferative activity of the columnar cells, the glandular pattern of the cervical mucosa changes in the intermenstrual period. In the early proliferative phase the glands are scanty, widely scattered in a dense, compact stroma. Their outline is regular, on cross section round or oval shaped, on longitudinal section tubular. The lumina are narrow and no secreting columnar cells are seen. In the late proliferative and in the secretory phase the number, size and shape of the glands undergo marked changes. The interglandular stroma becomes less and less, the glands are densely crowded, assume an irregular shape, revealing profuse branching and projections into the surrounding edematous stroma. The lumina become much wider, the lining columnar cells are seen bulging into the lumen and signs of secretion are present. Shortly before and at the onset of menstruation an extensive breakdown of the lining epithelium occurs. Some glands are seen entirely denuded, and after the exfoliation is completed the glands collapse and gradually reassume their regular outline with narrow lumina. A rapid regeneration follows and before the end of the menstrual period the cervical mucosa presents a normal histological picture. The stroma is a dense, fibrous tissue in the early postmenstrual period. The cells are widely spaced, the nuclei are small and there is very little cytoplasm in the stroma cells. The blood vessels are contracted. During the intermenstrual period an increased cellularity is noted, the stroma becomes edematous and loose and the blood vessels are engorged. The stroma cells change their forms and become larger with more cyto-

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plasm. In the secretory phase the stroma simulates an inflammatory condition.

Subsequent histological studies of the menstrual cycle confirmed these observations. A typical histological cycle could not, however, be observed in all of the cases, but a clear-cut cycle was found, involving uniformly all the tissue elements in about 70 per cent. In 30 per cent an exact determination of the menstrual phase was difficult. In the majority of these cases the cervical mucosa presented a confused histological picture in which glands characteristic of different menstrual phases were seen side by side. A certain overlapping of different histological phases in the same specimen is physiological, since the ovarian hormone action does not result in a uniform and simultaneous change in the mucous membranes. For the determination of the typical menstrual phase, it is essential that a generous piece of tissue be available for histological study. I also found specimens, in which the histological picture did not correspond with the known menstrual date, and believe that such a discrepancy is always suggestive of an imbalanced ovarian action. A normal menstrual history and apparently normal genital organs do not exclude the possibility of an abnormal ovarian function. In the case of anovulatory menstruation no clinical symptom indicates the true condition, except sterility. Persistent Graafian follicles containing active follicular hormones may also be present without initiating clinical symptoms, but the accentuated hormonal action and the absence of a corpus luteum is reflected in the histological pattern of the mucous membranes of the genital tract. An atypical histological cycle in the cervical mucosa is probably caused by ovarian dysfunction.

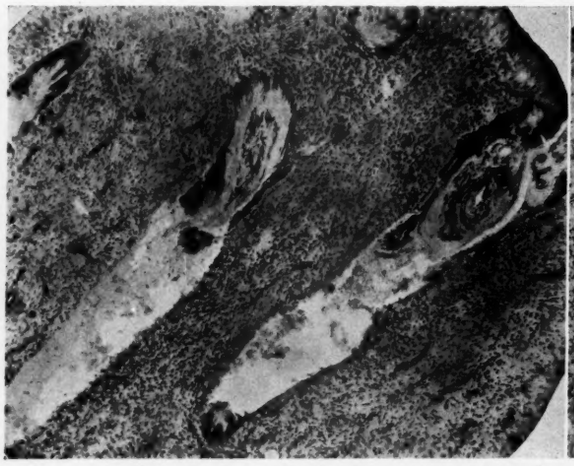

Fig. 1. Collapsed cervical glands partly denuded of their epithelial lining. The right side gland demonstrates the beginning re-epithelization.

Fig. 2. Almost entirely regenerated cervical gland. The lumen is filled with the exfoliated epithelium.

The cervical mucosa in the physiological menopause or after castration undergoes atrophic changes. The stroma becomes a dense connective tissue with pyknotic cells. The blood vessels are contracted and have unusually thick, muscular walls. The glands are regular in outline and have collapsed lumina. The lining epithelium in some of the glands is completely cast off, while in others the columnar cells reveal signs of pyknosis. Inactivity and gradual disappearance of the columnar epithelium is the outstanding feature in the cervical mucosa after the cessation of ovarian function. In physiological menopause, since the ovarian hormone production may continue for a long while after the cessation of menstruation, remnants of active columnar cells may be found in the mucosa many years after the clinical onset of the menopause. After surgical castration, however, the atrophic changes progress rapidly.

After my reports on the histological cycle, Sjövall[4] investigated human cervices removed by surgical operations or at autopsies. He studied the cyclic changes in thirty-four cervical specimens, nine of which were obtained at autopsies, six after supravaginal hysterectomies and sixteen from cases in which cervical biopsy was indicated by some cervical pathological condition. His conclusions were, that the human cervical mucosa is under ovarian hormonal influence, like the rest of the genital tract. He believes, that the proliferation of the columnar cells culminates in the early secretory phase and not later as described by the author. He was unable to ascertain a tissue loss at the time of menstruation. According to his observations, the cyclic transformation in the cervical mucosa is synchronous with the changes in the endometrium and in the ovaries. In eight cases of secondary amenorrhea with atrophied endometria, and in fourteen cases of cystic glandular hyperplasia of the endometrium he found identical histological changes in the endocervix. In childhood and after the menopause he found the cervical mucosa inactive.

Sjövall's description of the histological cycle can not be accepted in all its details without certain reservations. His specimens were obtained from pathological material, and his contention, that genital diseases, such as myomas and carcinomas, do not influence the normal cycle, is contrary to my observations. I firmly believe, that conclusive data of the normal cycle can be obtained only by the study of cervical specimens taken from normally menstruating women with apparently normal genitalia.

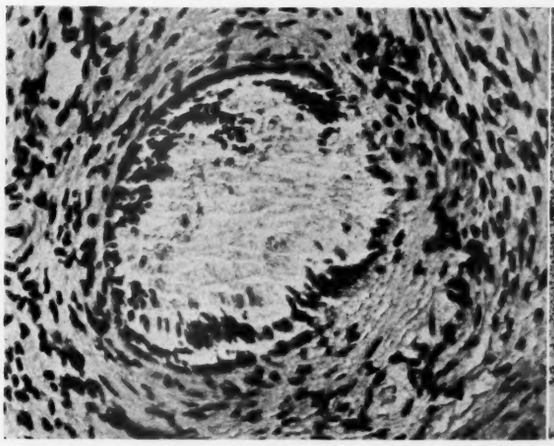

Fig. 3. Cross section of a cervical gland demonstrating a simultaneous process of exfoliation and regeneration.

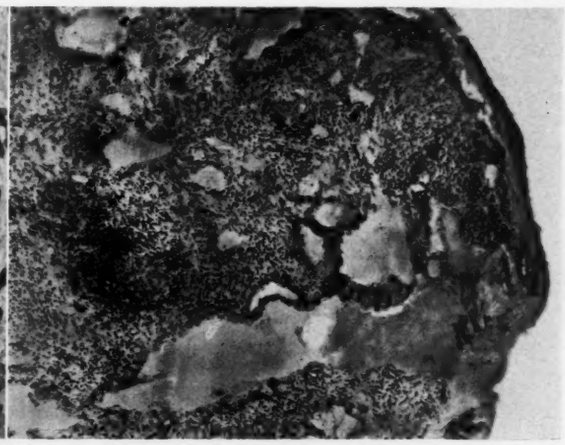

Fig. 4. Cervical stroma with engorged blood vessels, some of which opened up on the surface.

The loss of tissue incidental to menstruation was demonstrated in previous papers. In an additional four cases, in which a cervical specimen was secured from normal women immediately before or during the menstrual flow, I subjected the specimens to a painstaking histological study on serial sections. One specimen was obtained one day before the expected menstrual date. The serial sections revealed an overwhelmingly late secretory phase, but some glands were seen in the process of exfoliation and simultaneous regeneration. This observation seems to indicate that exfoliation and regeneration may begin in the mucous membrane before the clinical onset of menstruation. In two cases cervical specimens were taken at the beginning of the menstrual flow. Both specimens presented a similar histological picture. Extensive loss of tissue was noted in the cervical glands. In the serial sections, glands typical of the late secretory phase were found side by side with exfoliating, completely denuded and regenerating glands.

In the edematous stroma enormously dilated blood vessels filled with erythrocytes were seen. Blood was also found in the lumina of the glands, accompanying the process of exfoliation. In the fourth case, the cervical specimen was obtained on the third day of the menstrual flow. The mucosa revealed a completely regenerated histological structure. It is evident, therefore, that the process of exfoliation and regeneration is completed in the cervical mucosa before the end of the clinical menstruation.

The following photomicrographs illustrate some recent observations. They were taken from different sections of the same specimen, obtained on the first day of menstruation. Figure 1 demonstrates glands partly denuded, with the lining epithelium still clinging to the surface in some areas. Erythrocytes are seen in the lumen of the glands. In the gland on the right side of the picture regenerating epithelium is seen in a small area, revealing numerous mitoses. Figure 2 is the picture of an almost entirely regenerated gland. In some areas, however, the lining epithelium is still in the process of exfoliation, and the lumen is filled with desquamated epithelium. Figure 3 demonstrates the cross section of a gland under high power. It shows the simultaneous process of exfoliation and regeneration within the gland. Figure 4 includes a part of the stroma with engorged blood vessels, one of which is opened up on the surface. The surface epithelium is exfoliated.

The author's personal histological observations incidental to menstruation can be summarized as follows: Immediately before and at the beginning of menstruation there is an extensive loss of tissue in the cervical mucosa involving the columnar epithelial elements. Exfoliation and regeneration occurs simultaneously in the glands, and with such rapidity, that the process is probably completed within twenty-four hours. Before the end of the menstrual flow an entirely regenerated mucous membrane is present. The destructive process is accompanied by bleeding. Free blood is found in the lumina of the exfoliating glands, and some of the tremendously dilated blood vessels near the surface are seen opened up after the exfoliation of the surface epithelium. This observation seems to indicate that the cervical mucosa contributes to the loss of blood during the menstrual flow.

Since the ovarian hormones govern the biological function of the human cervical mucosa, an investigation of the possible rôle of these hormones in the production of pathological changes is indicated. The most frequent cervical pathologic alteration is endocervicitis. The clinical diagnosis of this condition is based on the presence of a copious discharge from the cervical canal Histologically, endocervicitis is characterized by an abundance of secreting cervical glands, and the amount of discharge is proportionate to the number of the glands. The development of the glandular structure in the endocervix is dependent upon the follicular hormone action. In the normal menstrual cycle, concomitant with the increasing hormone production in the ovaries, a gradual increase in the number and size of the cervical glands is noted. This observation was confirmed by Sjövall.[4] In cases with hypofunctioning ovaries an underdeveloped glandular structure is found in the endocervix, and in these cases cervical discharge is either entirely absent or scanty. After the cessation of ovarian function the cervix becomes atrophic and dry. In a series of castrated women I was able to reactivate the atrophic cervical mucosa by the administration of estrogen.[5] The columnar cells were stimulated to new growth, and by the administration of large doses of estrogen glandular hyperplasia with the clinical symptoms of leukorrhea was produced in the inactive endocervix. Zondek[6] followed up the cervical changes in three patients after the administration of large doses of estrogen, and found in all of his cases a remarkable increase in the number and size of the glands. The results of ovarian hyperfunction are known as glandular hyperplasia in the endometrium.

Similar changes were observed in the cervical mucosa with resulting symptoms of cervical discharge.

Erosion, clinically, is a red area around the external os, simulating an inflammatory condition. Histologically, this area is covered with columnar epithelium which is an extension of the endocervical surface epithelium. The occurrence of cervical erosions is fairly constant from the time of birth to the age of menopause, irrespective of infections. After the cessation of ovarian function they gradually disappear. In two menopausal women, who received moderate doses of estrogen continuously over fourteen and eighteen months, respectively, I observed the gradual development of an erosion in the dry, atrophic cervix. After the discontinuance of the hormonal treatment these erosions completely disappeared. Zondek[6] reported in one case the production of a large, partly papillary erosion after the administration of large doses of estrogen. He believes that an erosion of the portio can be caused by hormonal irritation.

Endocervicitis and cervical erosion can be produced in women by excessive hormonal stimulation. It is erroneous, therefore, to regard these cervical changes indiscriminately as the result of an infection. My clinical and histological observations indicate that glandular hyperplasia in the endocervix, and an active proliferation of the endocervical surface epithelium onto the portio, both caused by hormonal irritation, favor the invasion of infectious agents into this structure. Consequently, these hormonal derangements are frequently associated with infection. There are numerous cases, however, in which infection is absent, and the clinical syndrome of endocervicitis and cervical erosion is present only as the manifestation of a hormonal dysfunction.

Atypical epithelial proliferations may be initiated in the human cervical mucosa by hormonal irritation.[7] Up to the present time epithelial metaplasia was interpreted in the endocervix as a healing phase in erosions. The theory was, that the squamous epithelium growing back to the denuded surface, in its proliferation surrounds and invades the ducts of the glands. It was also believed that this invasive growth eventually becomes displaced to the surface where it belongs after the healing process is completed. My histological observations in a great number of erosion cases do not seem to substantiate this conception. If the healing process were the etiological factor for epithelial metaplasia, we should be able to find this histological picture in almost every case of erosion. In my material, however, I found it only in rare instances. In a series of castrated women I was able to produce epithelial metaplasia in dry, atrophic cervices by hormonal stimulation.[7] The importance of the hormonal etiology of epithelial metaplasia lies in this pathological condition's possible relationship to the development of carcinoma. Investigations into early cases of cervical carcinoma which were subjected to a painstaking histological study on serial sections, suggest that atypical epithelial proliferations probably present the first developmental phase in carcinoma.[8,9,10]

CONCLUSIONS

Extensive studies on the human cervical mucosa ascertained a histological cycle in this structure which is similar to that observed in the endometrium. The results of these experimental studies suggest that hormones play an important rôle in the production of those cervical disorders, the etiology of which is now obscure.

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METABOLIC EFFECTS OF THE ANESTHETIC AGENTS*

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BEFORE the anesthetist puts his patient to sleep, it is important that he know what effect the drug or drugs he is going to use will have upon that particular individual's metabolism both during and after the operation. It is the duty of the anesthetist to maintain the physiological "status quo" of his patient. It is with these thoughts in mind that we present the following review of the literature.

BASAL METABOLIC RATE

McKesson and Clement[42] have brought forth inadequate evidence from experimental work on the dog and from observations in man that the metabolic rate is very depressed by ether, less by nitrous oxide and least by ethylene.

Tribromethanol (avertin), in moderate doses, lowers the metabolic rate about 15 per cent[27] and, therefore, may be helpful in bringing the metabolic rate closer to normal values in cases of hyperthyroidism and marked apprehension.

It is imperative for the anesthetist to remember that an increased metabolic rate (seen with fever, pain, fear, hyperthyroidism, alcoholism, pregnancy and in young muscular adults) goes hand in hand with increased oxygen consumption and oxygen need. He should also be alert to the danger of anesthetic overdosage in patients with a subnormal metabolic rate (in the very young and very old, hypothyroidism, cachexia, prolonged illness, severe anemia, shock, jaundice and obesity).

BODY TEMPERATURE

Watkins and Wilson[86] anesthetized twenty-seven patients with ether administered by the open drop method, and found that eight minutes after the induction began the rectal temperature began to fall; the most rapid fall was in the first thirty minutes. The average fall was 1.8°F. during the first hour, and 0.8° the next hour. They noticed that the temperature fall was more rapid if the anesthesia was light. In the very ill patients, the temperature tended to rise toward the end of surgery.

Under ethylene anesthesia there is a very slight temperature decrease.[7]

Avertin produces a fall in body temperature,[27] which fits in with the picture of general metabolic depression that is produced by this drug. Furthermore, in 1894, Harnack and Meyer[28] reported that amylene hydrate, in which avertin is dissolved, also lowers the body temperature.

Evipal lowers the temperature.[33]

Heat may also be lost by allowing the expired air to escape into the room, which occurs when anesthetics are administered by the open drop method. This factor is negligible when the closed absorption system is used. Too much exposure of the skin and an increase in peripheral blood flow result in heat loss through radiation. Depletion of the glycogen reserve and circulatory depression lead to diminished heat production.[5]

LIVER

Ether. Liver function tests show that during ether anesthesia hepatic function is diminished, but returns to normal within twenty-four hours.[1,71] Almost always we find a hyperglycemia occurring, and the blood sugar level may rise to two or three times its normal value, the greatest rise occurring during the first hour. There is increased glycogenolysis in the liver, and probably an inhibition of insulin activity. This marked hyperglycemia is closely

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related to the amount of epinephrine being secreted and stimulation of the sympathetic nerves to the liver, for section of the hepatic nerves or adrenalectomy prevents almost completely a rise in the blood sugar.[62]

In both man[1] and in laboratory animals[49] the secretion of bile is depressed by ether anesthesia, though an occasional animal may secrete bile copiously.

Adriani[1] states that urea formation is normal under ether anesthesia, unless liver damage is present, which results in increased urea formation. However, Bollman[6] and Mann[48,49] claim that there is a moderate increase in urea formation which is in evidence in both the blood and urine. Moreover, the production of urea is not depressed, even in a severely damaged liver, because only a very small amount of hepatic tissue can produce large quantities of urea.

The activity of the reticular endothelial cells (Kupfer cells) is also depressed.[1]

Chloroform. Rosenthal and Bourne,[71] using bromsulfalein dye, tested the hepatic function of dogs after chloroform had been administered for only thirty minutes and found that impaired elimination of the dye could be detected for eight days. If chloroform were given for two hours, elimination was subnormal for six weeks.

The elevation of the blood sugar is greater with chloroform than with ether, and it is suggested[15] that this may be due to some extent to the direct action of the drug on the hepatic cells. Within the first half hour the hepatic glycogen is three-fourths depleted. However, the blood sugar level is again normal within twenty-four hours.

Acute fatty degeneration of the liver, heart, kidneys and other organs may follow prolonged chloroform anesthesia. Within a few days the patient may become very ill, have severe nausea and vomiting, become jaundiced, and then lapse into coma. This clinical picture of "delayed chloroform poisoning" or "postanesthetic toxemia" is usually ended by death. These symptoms develop from the first to the third postoperative day, and the laboratory findings show a severe toxic hepatitis. Due to the failure of prothrombin formation by the injured liver a hemorrhagic tendency is also seen. At autopsy a hepatic necrosis about the central vein is found.[27] If the patient recovers, no residual liver damage is observed, due to the tremendous regenerative powers of the liver cells and not to the choice of anesthetic agent.

This picture of chloroform poisoning can be prevented to some extent by adequate oxygenation during the course of the anesthesia and by a high carbohydrate, high protein and low fat diet prior to anesthesia. Goldschmidt, Vars and Ravdin,[26] and Miller and Whipple[55] believe that the best protection is given by a plenitude of protein stored in the liver.

Divinyl Ether (Vinethene). Though vinethene is less toxic than chloroform, it can also produce central lobular necrosis of the liver.

Goldschmidt and his associates[24] state that "the duration of the divinyl ether anesthesia was thus found to be a definite factor in the production of liver necrosis in the dog." They[25] also showed that oxygen lack during vinethene anesthesia contributes in great measure to hepatic damage. Ravdin and this same group[66] have emphasized that if vinethene is given with oxygen in cases lasting over forty-five minutes, no liver damage occurs.

However, Orth and his associates[60] have shown in dogs that prolonged usage or frequently repeated short anesthesias with divinyl ether will produce liver damage in spite of adequate oxygenation. This group reported, in 1941,[30] a toxic hepatorenal syndrome in a patient following the second of two administrations of vinethene that were ten weeks apart and lasted forty minutes and 104 minutes, respectively.

From the above evidence it appears that the liver can be safeguarded during vinethene anesthesia by using it only for short cases,[51,66,67] avoiding repeated usage on the same patient, adequate oxygen and a high

carbohydrate, high protein and low fat intake prior to anesthesia.[26]

Ethyl Chloride. Ethyl chloride is a halogen containing hydrocarbon, and therefore is capable of damaging parenchymatous organs. However, the drug does not have a widespread usage, and when employed it is only for very brief cases.

Ethylene and Nitrous Oxide. These drugs do not depress liver function or harm hepatic tissue unless anoxia is present.[1]

Cyclopropane. Raginsky and Bourne[65] have shown that cyclopropane does not diminish the functional capacity of the liver.

Tribromethanol (Avertin). Coleman,[16] using bromsulfalein dye tests, reported that hepatic function is diminished more frequently with avertin than with nitrous oxide or ether anesthesia.

Avertin combines with glycuronic acid in the liver and is excreted by the kidneys. There is little serious effect seen from the doses used in basal anesthesia. However, if liver damage is already present, the conjugating rôle played by the liver assumes very great importance. Beecher's[5] perfusion experiments portrayed this very clearly: a 420 Gm. normal dog's liver reduced the blood concentration of avertin from 130 mg. per cent to 6 mg. per cent in ninety minutes, but a liver in which fatty degeneration was produced experimentally was only one-half as efficient. The same is seen clinically when dangerously prolonged anesthesia results from avertin used in patients with known liver damage.

Adriani[1] states that cloudy swelling is the only pathological change, and Bourne and Raginsky[11] observed in animals that large repeated doses are required to produce hepatic damage, which is only moderate in degree and reversible.

Kobayashi[35] found a marked increase in the bile flow of dogs under both avertin anesthesia and avertin amnesia or sedation. Epinephrine, insulin, atropine, blockage of the reticulo-endothelial system, and concentrated glucose solution given orally did not influence the bile flow. Therefore, he concluded that the augmented bile flow was the result of the direct action of the avertin upon the liver cells.

Barbiturates. Anesthetic doses of the barbiturates decrease liver function and decrease the liver glycogen.[1] However, Atnan and Fenz[2] report that evipal does not produce any disturbance of the blood sugar in diabetics.

It is believed that the comparatively brief anesthesia produced by a single dose of an ultrashort acting barbiturate is due to the rapid side chain oxidation of the drug in the liver. However, the proof that these drugs are destroyed in the liver is all indirect. Patients with poor liver function have remained anesthetized for many hours from a dose of evipal which in normal individuals results in only fifteen minutes of anesthesia. Koppanyi and his associates[36] have shown that rabbits and cats who were given pentobarbital and phenobarbital twenty-four hours following recovery from two hours of chloroform anesthesia, remained deeply depressed for a long time; occasionally, some of the animals died from doses that were only one-half the average fatal dose. Similar results have been obtained with evipal in dogs.[50]

Reynolds and Veal[69,70] state that the continued administration of pentothal to animals in doses just adequate to maintain light anesthesia will eventually produce signs of heart muscle poisoning and circulatory collapse. The first dose of pentothal produces a few minutes of anesthesia, and subsequent doses, given before complete recovery, result in lengthening periods of anesthesia indicating that the drug is cumulative and is not rapidly and completely destroyed. Kozelka and Hines[37] have confirmed this work. Furthermore, in studying the chemical fate of pentothal in the body, they were unable to demonstrate the drug in the tissues after ten minutes. Pentothal and its oxygen anologue, pentobarbital, could not be shown even during profound depression. If enough pentobarbital had been given to produce a simi-

lar degree of anesthesia, the drug could have been found in the tissues. They, therefore, conclude that pentothal produces its cumulative effects through the accumulation of some unrecognized degradation product.

We can only surmise from the above that barbiturate anesthesia and the liver are closely related, but that the exact mechanism is not known.

Procaine. Thieulin[78] found that procaine is converted into para-aminobenzoic acid and di-ethyl-amino-ethyl alcohol. Very little procaine is excreted as such by the kidney, and it is believed that almost all of it is detoxified in the liver.[29] Ellinger and Hof,[21] working with the belief that the liver is the site of detoxication, produced hepatic damage in cats with chloroform, and then showed that these cats had greater susceptibility to intravenous procaine than the healthy controls.

Dunlop[20] observed in dogs that procaine, when injected into the blood stream, is rapidly broken down into nontoxic end products which are slowly excreted by the kidneys, and that though many tissues possess the ability to detoxify procaine, none can do it as quickly as the liver. He, therefore, believes that there are theoretical grounds against the use of large amounts of procaine in patients with severe liver damage.

KIDNEY

Beecher[5] states that anoxia rapidly damages the colloidal membrane of the kidney, the glomerular epithelium, and allows it to become permeable to protein, albumin and blood; that an increase in both general arterial pressure and renal blood flow (seen with carbon dioxide excess and oxygen lack) results in an increase in urine formation; that a marked blood pressure fall may greatly diminish urine secretion, and occasionally stop it entirely.

Ether. Urine formation is depressed in varying degrees by ether anesthesia. Pringle[64] and Walton,[83] in humans and dogs, respectively, have shown that the production of urine is inhibited by ether anesthesia. In 335 patients who were undergoing operation and were anesthetized with ether, Miller and Cabot[56] observed that the efficiency of phenolsulfonthalein excretion was decreased on an average of 18.8 per cent, and that excretion returned to normal in twenty-four to forty-eight hours.

Ether is believed to be a sympathetic stimulant, and it is possible that constriction of the renal vessels is the cause of the diminished urine output. In animals that have undergone unilateral renal sympathectomy, the denervated kidney excretes as well under ether anesthesia as when the animal is awake, but the output of the intact kidney decreases.[5]

MacNider has done some classical work on the effect of ether anesthesia on urine formation. He found[43] that when anuria occurred in animals under ether anesthesia, it was a temporary anuria which occasionally became permanent, it occurred one to two hours after the beginning of anesthesia, and it was frequently accompanied by a drop in the blood pressure. The administration of either normal saline or 1 per cent theobromine solution re-established the urine flow. He also showed that age is an important factor. Both young and young adult dogs showed only a very slight impairment of urine formation when anesthetized with ether for two hours. However, the older animals, after one hour of etherization, showed either an oliguria or an anuria with the urine containing albumin and casts. Furthermore, the alkali reserve of the blood was reduced, whereas it was unchanged in the younger dogs.

Upon further study, MacNider[44] discovered that in the renal epithelium and in the glomerular capillaries of the older dogs there was present much more stainable lipoid material. To rectify the disturbance of the acid-base balance, dilute sodium bicarbonate or glucose solutions were given intravenously prior to anesthesia;[45] and it was found from biopsies taken under local anesthesia that the amount of lipoid substance was greatly diminished. After

such intravenous therapy the older animals could be anesthetized with ether for two hours without showing any signs of kidney damage or dysfunction. An increase of lipoid material within the renal epithelium of pregnant animals also seems to be the cause of their susceptibility to ether.

Nitrogen excretion is increased for twenty-four to forty-eight hours after ether anesthesia.[31] The phosphorous output rises,[8] as does the amount of ascorbic acid that is excreted. Glycosuria and ketonuria are frequently present.

Chloroform. MacNider[43, 46, 47] found that by the time the induction with chloroform was complete, the dogs were frequently anuric, and by the end of the first hour all the dogs had anuria. A notable decrease in the alkali reserve of the blood was frequently present, and here the use of diuretic solutions were of no avail in inducing a flow of urine.

Upon studying the effect of a two-hour chloroform anesthesia on pregnant dogs, MacNider[46] observed that a preliminary injection of glucose failed to afford any protection, and that the effects were more harmful in the older animals and in the more advanced pregnancies. The tubular epithelium suffers most of the damage,[43] and occasionally hemorrhages are found. Similar changes are seen in the human kidneys.[32]

In man the excretion of urea, uric acid, creatinine and ammonia is increased, but hippuric acid is decreased.[31]

Cyclopropane. Waters and Schmidt[84] have shown that cyclopropane depresses renal function only temporarily, and that this is followed by a compensatory increase of short duration.

Divinyl Ether. Vinethene anesthesia results in a progressive diminution of renal activity in dogs and may go on to complete anuria.[60]

Tribromethanol. In 1931, Veal and his associates[82] noted that in normal rabbits there was a large margin of safety in an anesthetic dose of avertin; but if a very mild nephritis is produced first, the margin of safety disappears. This may be due to renal failure in eliminating the tribromethanol glycuronate formed in the liver.

Avertin seems to depress urine formation,[14] but does not damage the normal kidney,[58] though 14 to 20 per cent of the patients may show a transient albuminuria.

Under avertin-nitrous oxide-oxygen anesthesia the blood urea rises about 3.4 mg. per cent,[5] but goes much higher in older patients.[63]

Ethylene and Nitrous Oxide. Unless anoxia is present, renal activity is not altered.[1]

Barbiturates. Large doses of barbiturates produce an antidiuretic effect due to action centrally on the hypophyseal-pituitary system.[27]

Those barbiturates which are not broken down in the liver are eliminated by the kidneys. Since renal excretion occurs rather slowly, those drugs (barbital, phenobarbital) which depend upon the kidneys for elimination, manifest a longer duration of activity. Hence, when renal function is impaired, these long acting barbiturates may cause severe depression and poisoning.

GASTROINTESTINAL TRACT

During the induction of anesthesia the odor and taste of the drug may produce salivation, nausea and vomiting. The emesis may be due to the irritating action of the anesthetic agent on the gastric mucosa.

Payer[61] noticed in humans that after anesthesia almost all cases showed some amount of gastric dilatation. In uncomplicated cases this dilatation lasts from twelve to twenty-four hours even though no symptoms may be present. However, when gastric symptoms are present, the stomach is also found to be relaxed for several days.

Ether. Experimental and clinical evidence points to ether anesthesia as being a cause of postoperative gastrointestinal symptoms. Beecher[5] states: "In the surgical stage of ether anesthesia almost com-

plete inhibition of the smaller contractions occurs; peristalsis is entirely abolished in the stomach, small intestines, and colon. A distinct loss of muscular tone occurs in these regions."

Chloroform. The effects of chloroform are similar to those of ether, but, in addition, there is a tendency to bleed into the serous membranes.[32]

Ethylene. There is very little effect produced on the gastrointestinal tract by ethylene and oxygen anesthesia.[53,54,61]

Nitrous Oxide. This agent does not seem to alter gastrointestinal activity. However, if anoxia is present an increase in the size of the contractions of the stomach, ileum, and colon (dogs) follows.[53,54]

Divinyl Ether. Molitor[57] believes that vinethene does not interfere with the automatic movements of the intestines. However, Burstein[15] has shown in dogs, and the work has been confirmed by Orth et al.,[60] that vinethene diminishes gastrointestinal muscular tone and inhibits intestinal contractions completely in all planes of surgical anesthesia.

Cyclopropane. During anesthesia with cyclopropane the intestines are contracted and active, which may be due to the possibility that this agent is a parasympathetic stimulant.

Waters[85] analyzed 10,638 cases and found the incidence of postoperative distention to be as follows: nitrous oxide, 3 per cent; ethylene, 7 per cent; cyclopropane, 13.5 per cent; ether 16.5 per cent.

Barbiturates. The barbiturates seem to decrease the intestinal activity, but this is not believed to be as marked as with ether.

PANCREAS

Zucker and his associates[87] studied the blood amylase in man under anesthesia and found that ether produced a rise to two or three times the normal value. However, the blood amylase became normal within twenty-four hours.

Avertin did not produce any change in the blood amylase.[87]

SPLEEN

Under ether anesthesia the intact spleen of the dog decreases in volume as much as 50 per cent.[4,22,72,73,74] However, the denervated spleen does not constrict, showing that the sympathetic nervous system does play a major rôle in maintaining the splenic volume. This is also implied when the spleen of the dog increases to four or five times its normal size under spinal anesthesia.[17] The variations in the blood pressure and the depth of the anesthesia are also important in controlling the size of the spleen.

All evidence points to the barbiturates as causing splenic dilatation.[22,72,73,74]

BLOOD

Leucocytes. The father of modern physiology, Claude Bernard, first discovered that anesthesia produces a leucocytosis. All the agents raise the white count, and this is most marked with ether[23,52] and cyclopropane.[77] The total white count rises, and the differential count shifts greatly to the left. The increase in the white blood cells begins with the anesthetic induction and attains a peak in four to eight hours, at which time, depending upon the duration of the anesthesia, it may be two or three times the original count; furthermore, it is three to five days before the count returns to its normal level.

Boyd[12,13] showed that ether anesthesia diminishes the phospholipid content of the leucocytes, indicating that there is a chemical difference between the leucocytosis of disease and anesthesia.

Erythrocytes and Hemoglobin. The red blood cell count, the hemoglobin concentration and the hematocrit value increase under ether anesthesia.[72] Essex et al.[22] believe that this is due to the erythrocytes which are injected into the circulation by the profound contraction of the spleen; splenectomy abolishes this blood concentration. The reduction in plasma volume is another cause for the hemoconcentration.

Ether also increases the sedimentation rate of the red blood cells.[38] The platelets are increased by 78,000 per cu. mm. of blood in dogs.[72]

Cyclopropane does not effect the erythrocyte count.[77,84]

According to Bruger and his coworkers,[14] avertin produces a slight rise in the red cell count in dogs. However, Tiba[79,80] claims that there is a 70 per cent decrease in the red count after thirty minutes of avertin and that the sedimentation rate is decreased.

The barbiturates produce a marked dilatation of the spleen and a dilution of the red blood cells which may be sequestered in that organ.[10,22,72,73,74] Dallemagne,[18] while working on dogs observed a severe anemia and a fall in the oxygen carrying capacity of the blood from 21 to 9 volumes per cent as late as twenty-four hours after the use of evipal. With repeated anesthesias the anemia became aggravated. As yet, however, there has not been any confirmation of this work in man.

Blood Volume and Water Balance. McAllister[40,41] has shown in dogs that ether anesthesia causes a reduction in the blood plasma volume but no marked changes in intracellular or extracellular water. Stewart[76] has found an average reduction of blood plasma volume of 14.3 per cent in humans under ether anesthesia. However, Barbour[3] found no change in the plasma concentration in two carefully controlled periods of ether anesthesia in two rabbits, and, therefore, he believes that ether anesthesia need not produce water shifts into or out of the blood. This does not agree with McAllister[40,41] and Stewart,[76] but the difference may be due entirely to the different animals used in the experiments. We do know that etherization produces hemoconcentration which probably follows the extrusion of erythrocytes from the spleen into the circulation.[4,22,72,73,74]

The barbiturates cause a decrease in the concentration of the blood. This is due to the movement of some of the red blood cells into the spleen and the addition of a great deal of water to the plasma, most of it coming from the intracellular fluids with the cerebral cortex and liver making large contributions.[3]

The gas anesthetics apparently do not cause any great shifting of the body water. However, with third plane and deeper anesthesia, the reflexes controlling water balance, blood volume and heat regulation may be obliterated;[3] consequently, the physiology of these mechanisms becomes pathological.

Acid-base Balance. There is no agreement among the men who have worked on this subject as to what occurs to the acid-base equilibrium during anesthesia. However, the opinion of most is that an acidemia is produced by general anesthesia.[81] Dallemagne[19] after an extensive review of the subject concludes that "no law governs the variations of the acid-base equilibrium after the administration of anesthetics."

Cholesterol. A rise in the blood cholesterol of 50 to 100 per cent occurs during ether anesthesia, the increase paralleling the duration of the anesthesia, until a peak is reached in sixty to ninety minutes. The values return to normal in four to five hours. This increment in the blood cholesterol goes hand-in-hand with the rise in the blood sugar; however, both substances will remain at almost normal levels if insulin is given several hours prior to the anesthetic. In diabetics though, there does not exist such a relationship between the blood cholesterol and glucose.[5]

Chloroform produces a 5 to 10 per cent rise.[5]

Ethylene, nitrous oxide and the barbiturates do not produce any rise unless the patient undergoes an excitement stage.[5]

Nonprotein Nitrogen. The blood urea increases slightly under ether and chloroform anesthesia.[6,34,48,49] The blood ammonia increases 10 to 50 per cent under ether.[74] Cyclopropane does not produce any changes.[59]

CONCLUSIONS

It is obvious that rarely is there a need for chloroform in the anesthetist's armamentarium, because of its dangerous metabolic effects. Ether, which is supposed to be our safest anesthetic agent, produces marked metabolic disturbances, which, though only temporary in nature, may be most harmful to the very ill patient. Of great importance is the fact that cyclopropane is almost innocuous to the body metabolism.

When vinethene or chloroform are administered by the open drop method, the patients should be given additional oxygen by either the oral or nasal route. Vinethene should not be used for long procedures, and should not be used too often on the same individual.

Avertin should not be employed in cases of hepatic or renal disease, in patients with a subnormal metabolism, or in elderly patients who frequently have potential kidney dysfunction and whose physiological functions will not withstand further depression.

The barbiturates, which are being used more extensively, need further investigation. The possibilities of anemia, myocardial damage and circulatory depression lack clinical confirmation. This group, when used for purposes of premedication or in conjunction with other anesthetics, may be helpful in preventing shock by maintaining the blood volume and in counteracting the hemoconcentration produced by ether. The latter can also be done by morphine[9] and codeine.[3]

When procaine is used indiscriminately in the presence of known hepatic damage, it may be that failure of the liver to detoxify the drug rapidly will result in the dangerous situation of a large amount of pure procaine being present in the circulation.

A high carbohydrate, high protein and low fat diet prior to anesthesia may help protect the liver, diminish nausea and vomiting and guard heat production. It is possible that a small or moderate dose of insulin given several hours before anesthesia may help avoid excessive glycogenolysis. Intravenous glucose or dilute sodium bicarbonate solutions prior to anesthesia may protect the kidneys of elderly patients.

Blood counts and blood analyses done on blood that is drawn during anesthesia and the first few days thereafter must be considered carefully, because the agent used may produce many variations from the normal.

There are a tremendous number of problems to be solved. It is hoped that as much as possible will be done under clinical conditions, in the operating room, for human physiology varies greatly from animal physiology, and a sick patient undergoing operation differs in many respects from a healthy animal, the subject of a controlled laboratory experiment.

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A SIMPLE PLASTIC PROCEDURE OF THE FINGERS FOR CONSERVING BONY TISSUE AND FORMING A SOFT TISSUE PAD

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THIS procedure is to move a section of palmar surface skin to the amputated end of the finger. It has been suggested that this method has appeared in the literature. The writer has been unable to find it.

FIG. 1. Drawing illustrates line of incision forming palmar skin section.

In America's large industrial plants, amputation is approaching a rarity. In the smaller jobbing shops, where safety departments are less efficient, this injury is still sadly common.

The writer has had rather discouraging results with the free graft in industry. Needless to say, all digit amputations will not submit to this plastic operation. Generally speaking, an amputation through a nail, if the proximal part of the nail or its bed, remains and if the transverse line of amputation is not too oblique with the long axis of the finger, the operation has a good chance for success.

PROCEDURE

On admission to the plant hospital the base of the finger is cleansed with benzine, green soap, alcohol and mercresin, care being taken not to get any of these into the open wound. Then 1 per cent novocaine is injected at the base of the finger, about 2 to 2½ cc. in each side, using care to get enough near the dorsal aspect of the finger. Rarely is more than a total of 5 cc. required.

Following this the lesion is scrubbed with green soap as is the remainder of the finger. This is followed by alcohol and mercresin after which the arm, hand and finger are draped. The wound is débrided.

The end of the remaining part of the distal phalanx is trimmed and the edges rounded and smoothed. Occasionally, the palmar edge may have to be trimmed back further than the extensor edge. This, of course, is determined by the débridement necessary. In some cases a small section of remaining distal phalanx may have to be removed.

Next a transverse incision is made on the palmar surface about 3/16 to ¼ inch, (6 to 7 mm.), proximal and parallel to the edge of the amputation. The incision is extended from the midlateral point on one side to the same point on the other side. (Fig. 1.) The depth of the incision is not difficult to determine. It is carried down through the layers of the skin and just into the areolar tissue. A transverse section or strip of skin is free to be moved over the end though it is still attached on both its lateral ends. Under-cutting is not necessary.

All that now remains to be done is to move the section distalward and dorsally so it covers the end of the finger. This is

easily done with three, rarely more, linen sutures. The sutures are passed through the nail or its bed, and through the skin section near the distal edge and drawn up tight under the nail or to the bed. The denuded area just proximal to the proximal edge of the skin section granulates in well and rapidly. The small scar formed, though it is on the flexor surface, is not tender and has caused no inconvenience. A vaseline gauze dressing covers the entire finger. The first dressing is done in five days and the sutures are removed about the eighth or ninth day. If removed too soon, the skin section will move toward its original position. The nail usually sloughs and a new one forms. The new nail will be shorter than its fellow and predecessor but will bear a proportional engtth to its finger.

Fig. 2.

Fig. 3.

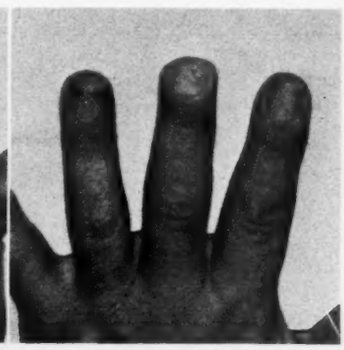

Fig. 4.

Fig. 2. Left second finger of Mr. T. M. on August 25, 1941, about five minutes after traumatic amputation.

Fig. 3. Left second finger of Mr. T. M. on September 26. Note difficulty in determining scar left by moving skin section.

Fig. 4. Left second finger of Mr. T. M. on September 26. Note small lateral distal fragment of old nail remaining.

The average healing time is twenty to twenty-five days with the disability depending on the patient and the ability of the department to place him for the first four to six postoperative days.

One possible failure out of twenty eight cases was noted:

J. W., a nineteen-year old female, factory worker, was operated upon in the manner described. However, in addition, a free split thickness graft was taken from the thigh and sutured on the denuded area. The graft did not take. The donor area healed as usual and required only sterile vaseline gauze dressings. After the graft sloughed the denuded area healed as usual. Three weeks after her discharge, she returned, complaining of pain at the tip of the finger. The pad was not as thick as usual due to lack of depth of the transverse palmar surface incision. However, it did not appear to be unduly thin. There was no evidence of an amputation neuroma. The patient was asked to give the finger a trial for some time, perhaps a month, and return to the clinic if she still had difficulty. She has not been seen since.

The remaining twenty-seven patients healed rapidly. The final results were similar to those shown in Figures 2, 3 and 4. Patients are eager to avoid loss of appreciable finger length and loss of the nail. The cosmetic result is happily accepted.

There seems to be evidence that grafting the denuded area is of no value in improving the final result or in decreasing the healing time. The writer prefers not to graft.

The risk to the operation is no greater than that involved in any nerve blocking procedure and the same precautions should be observed. In case of a failure the finger can be amputated and closed with a palmar flap.

CONCLUSIONS

A bone conserving plastic procedure is presented which is simple and requires no special skill or instruments.

Disability is not long.

There is little, if any, risk; and the final result is a good finger functionally and cosmetically.

Case Reports

GASTRECTOMY FOR CARCINOMA*

CASE REPORT OF OLDEST PATIENT TO SURVIVE

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TOTAL gastrectomy is becoming a more frequent operation. According to Finney and Rienhoff, Phineus

Fig. 1. Preoperative fluoroscopy revealing extensiveness of carcinoma.

Conner of Cincinnati performed the first total gastrectomy in 1884. The patient did not recover. However, in 1897, Schlatter performed the first successful total gastrectomy.

In 1929, Finney and Rienhoff collected from the literature sixty-seven cases of total gastrectomy, and Raeder reported eighty-eight cases up to 1933. Since that time the operation of total gastrectomy has become a more frequent occurrence. The Mayo Clinic reported twenty-seven total gastrectomies between 1907 and 1938, and sixteen since 1937. Arthur W. Allen, reporting the experience at the Massachusetts General Hospital, listed fifteen cases between the years 1932 and 1938. Lahey, in 1939, reported nine cases. Besides these, a number of single case reports have been published and it is known that other small groups of cases have not as yet been reported in the literature.

According to Walters, the indications for total gastrectomy for carcinoma are three: (1) The lesion should be confined entirely to the stomach without evidence of metastases. (2) The entire stomach and lower end of the esophagus should be sufficiently mobile to enable the surgeon to remove the stomach and to make the esophagojejunal anastomosis without too much difficulty. (3) The general condition of the patient should be good, so that the risk assumed is not too great.

The mortality rate, as might be expected, is high. Finney and Rienhoff reported in the collected group of sixty-seven cases a mortality rate of 53.8 per cent. Allen, in the group of fifteen cases from the Massachusetts General Hospital, reported 7 deaths. Lahey stated that in the nine cases of total gastrectomy, there were five surgically

* From the Department of Surgery, The Duluth Clinic, Duluth, Minnesota. Read before St. Luke's Hospital Staff Meeting, Duluth, October 16, 1941.

successful. According to Donald, in the Mayo Clinic series of twenty-seven cases between 1907 and 1938, there were only

Fig. 2. Gross specimen removed at operation.

nine survivals, or a mortality rate of 66⅔ per cent. However, in the sixteen total gastrectomies since 1937, the mortality rate decreased to 31 per cent.

The cause of death, according to Finney and Rienhoff, as one might expect, was peritonitis in 58 per cent, shock in 22 per cent, and miscellaneous causes in 20 per cent.

According to Waugh and Giffin in the *Proceedings of the Mayo Clinic* for June 4, 1941, a patient seventy-two years old, upon whom they had performed a total gastrectomy, represented the oldest person to undergo total gastrectomy successfully as far as they could ascertain from the literature.

I wish to present the following case of a man, age seventy-nine, as the oldest individual to undergo a successful gastrectomy for carcinoma.

CASE REPORT

W. S., age seventy-nine, consulted Dr. P. G. Boman, August 25, 1941, because of epigastric

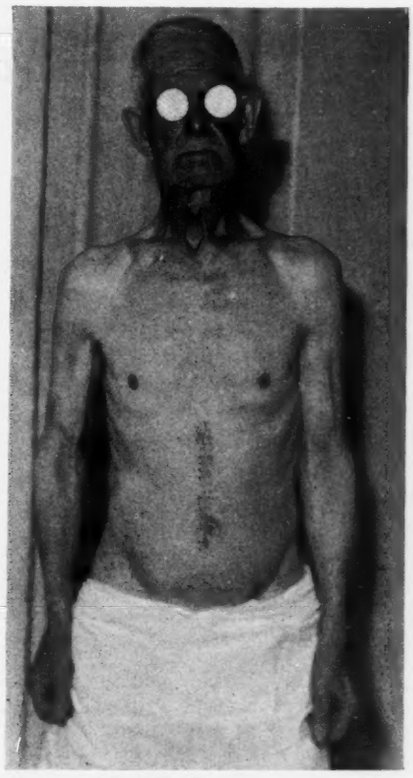

Fig. 3. Mr. W. S., age seventy-nine, seven weeks postoperatively.

pain and distress. This distress dated back three months. The pain was constant and dull in character. He had a poor appetite and had lost fifteen pounds in weight. There was also an associated weakness, and constipation.

The patient had first been seen in the Clinic in 1917, at the age of fifty-five. He then gave a history that for twenty-five years he had had stomach trouble. He was examined by Dr. T. R. Martin and found to have an achlorhydria. Stomach fluoroscopy was negative. He was treated with dilute hydrochloric acid.

In 1923, a bilateral herniotomy was performed by Dr. Braden. Following this he had a cystitis and prostatitis, and was under the care of Dr. Nicholson.

In 1927, he consulted Dr. P. G. Boman, because of stomach distress, and again it was found that he had an absence of free hydrochloric acid. A stomach fluoroscopy was negative. He was treated with dilute hydrochloric acid.

In 1937, he was treated for frequency of urination by Dr. Nicholson.

In 1938, he consulted Dr. Boman and it was found that he still had an absence of free hydrochloric acid. The stomach fluoroscopy, as before, was found to be negative. Treatment with hydrochloric acid was resumed.

Fig. 4. *X*-ray view of the esophagojejunal anastomosis twenty-seven days postoperatively.

In 1941, he was treated for a prostatitis by Dr. Nicholson.

Family and marital histories were irrelevant.

Examination showed this elderly man to be rather thin, weighing 120½ pounds. He showed evidences of weight loss. Despite this, he was quite well preserved for his years. There was some evidence of chronic emphysema. His blood pressure was 110/80. The heart and lungs were normal for his age.

Abdominal examination revealed a mass on fluoroscopy associated with the stomach (Fig. 1), which Dr. Boman believed to be an inoperable carcinoma of the stomach. Test meal revealed an absence of free hydrochloric acid and there was three plus occult blood present.

Examination of the blood showed the hemoglobin to be 12.5 Gm. or 85 per cent, the red blood count 4,510,000. The urine was negative for albumin and sugar.

The patient was told that he had an extensive carcinoma of the stomach which probably could not be removed. However, he and his family elected to have an exploration, and therefore he entered the hospital, September 1, 1941. September 3 he was explored.

Anesthesia was accomplished with ethylene and ether vapor. It was found that there was a diffuse carcinomatous involvement of the stomach extending from the pylorus almost to the esophagus. However, the stomach was not attached and there were no evidences of peritoneal or liver metastases. There were, however, a few enlarged glands in the gastrocolic and gastrohepatic ligaments. It was decided to attempt a total gastrectomy. The gastrocolic omentum was first divided along the greater curvature. The duodenohepatic ligament was then divided, and the duodenum cut across just distal to the pylorus. The duodenum was inverted. The attachments to the spleen were divided, which allowed for greater mobility. The right gastric artery was then divided and ligated. In this way, we were able to mobilize the cardia and the esophagus. A loop of the jejunum was brought up through the mesocolon, and an anastomosis was made with a layer of interrupted silk No. 1 sutures and two rows of No. 0 chromic catgut. The suture line was reinforced with omentum. A jejunojejunostomy was then performed. A gastro-enterostomy tube which had previously been inserted was then brought down through the anastomosis well along into the distal loop of the jejunum. Finally, the mesocolon was sutured about the loop of the jejunum. A penrose drain was inserted below the inferior surface of the liver. Two Gm. of sulfanilamide powder were left in the operative area and another 2 Gm. were placed in the wound during its closure. He was given 500 cc. of 5 per cent glucose and 1,000 cc. of citrated blood during the course of the operation. The operative procedure took almost three hours. At the close, his systolic blood pressure was 120 and the diastolic pressure 70.

Dr. A. H. Wells* submitted the following report on the gross specimen (Fig. 2):

"Specimen consists of a large mass of stomach, including about 2 cm. of the duodenum. When spread out it measures 20 cm. long and 12 cm. wide. The entire pyloric end, including

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the pyloric valve, over an area measures about 13 cm. in length is hard, diffusely and severely thickened, but apparently not extending into the duodenum. The mucosal surface over this area is fixed and gray. The submucosa and muscularis are uniformly indurated, gray, firm and thickened, averaging 1½ cm. in breadth. The serosa is likewise unusually gray and fixed to deeper tissues. At the fundal end there is apparently 5 cm. of normal appearing mucosa. There is no ulceration of the involved mucosal surface.

"Microscopic: There is a wild, very diffuse invasion throughout the various layers of the gastric wall by highly anaplastic and very small epithelial cells. Occasionally these cells form definite glandular structures.

"Diagnosis: Scirrhous carcinoma of stomach (N5-d2-ca. stomach)."

Feedings through the gastro-enterostomy tube were begun on the second day. For two or three days there was rather profuse drainage through and about the penrose drain, but this gradually decreased, and his wound healed without infection. The gastro-enterostomy tube was removed on the fifth postoperative day, and thereafter frequent small, oral feedings were given. He was allowed out of bed on the ninth postoperative day and left the hospital on the sixteenth postoperative day.

SUMMARY

A patient (age seventy-nine) is presented who was operated upon for carcinoma of the stomach. Total gastrectomy was performed. The patient made an uneventful convalescence and I believe is the oldest patient to survive this procedure. At the time of this writing, almost three months following operation, his recovery has continued to run a smooth course.

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MALIGNANT MELANOMA OF THE RECTUM*

REPORT OF A CASE

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THE exact origin and the significance of melanin in malignant melanomas is a matter of controversy. The uncertainty of its origin is shown by the presence of melanin in both carcinomatous and sarcomatous growths. Although melanin occurs normally in the choroid of the eye, in the skin and in the hair, and is found in fairly large amounts in certain new growths and in melanotic tumors, it is extremely difficult to obtain it in any quantity and in a purified form. Melanin is difficult to isolate since it does not crystalize and it is insoluble in fluids which do not change its composition. Melanin is soluble in a strong alkali or acid, which, however, changes its composition. This makes it extremely difficult to learn its exact chemical composition and presents a fundamental difficulty in studying melanin in normal and pathologic cells. An added difficulty is the presence of melanin in foods of plant and animal origin and its normal formation within the body. We often find melanin in the mucosa of the appendix, in the colon in chronically constipated individuals, and in the epithelium of the collecting tubules of the kidneys in adults.

It is believed that melanins are a group of nitrogenous compounds closely related to the proteins. Some believe that melanin found in tumors is purely of endogenous source, originating either from a special pigment cell, or from cells which have taken on the function of pigment formation. Dawson studied a number of benign and malignant melanomas, none of which occurred in the anus. "The term melanoma," he says, "emphasizes the specific character of the tumor cell, which contains a variable amount of an iron-free pigment, melanin. Color or pigment production in the animal kingdom, especially in the highly pigmented vertebrates, the frogs and reptiles, has long been held to belong essentially to a specific cell, the 'chromatophore,' and the claim of the exclusive relation of this cell to pigment production is only emphasized in the admission (*a*) that the overflow from the chromatophore may be transported to epithelial cells of the epidermis, and (*b*) the deposit of this excessive pigment from the mesoblastic chromatophore, in certain cells of the foetal epidermis may excite these cells to proliferate and cause them to assume the function of pigment production. The pigment cell, on the other hand, is held by others to have arisen from the ordinary connective tissue cell of the corium, or to be of endothelial origin, or again exclusively of epidermal origin, with the further contention that the connective tissue cells merely carry off the surplus in the lymph paths."

We may or may not admit the specific character of the cells which form the melanin pigment, but we all recognize the great variation in the histologic makeup of tumors containing the pigment. Even though we admit the source we still do not know the significance of the presence of the pigment in malignant tumors.

Chalier and Bonnet have analyzed sixty-four cases of melanomas of the intestinal tract and found that 2 or 3 per cent of all melanomas occur in this region, and that most of these are found in the rectum. They see a resemblance of these tumors to epidermoid carcinoma, and believe that these tumors are derived from the anal epi-

* Read before the American Proctologic Society, June, 1941, Cleveland, Ohio.

dermis and infiltrate beneath the mucosa. Ewing in his book on "Neoplastic Tumors" discusses and summarizes the theoretic origin of melanomas in a masterly manner.

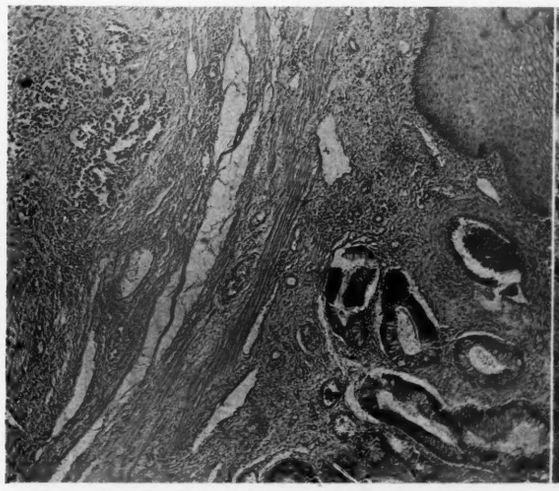

Fig. 1. Study of section of mass removed May 15, 1939. Stroma is the site of dense neoplastic infiltrative process consisting of single cells, groups of cells and irregular acini (lower power).

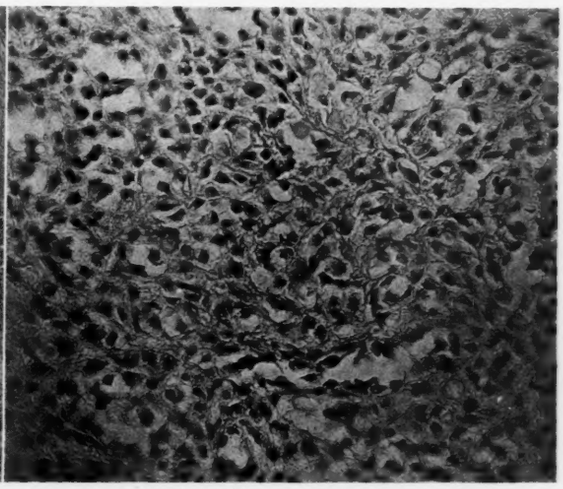

Fig. 2. Study of section of mass removed May 15, 1939. The cells show a marked variability in size and shape of nuclei; innumerable mitotic figures are present (high power). Diagnosis: anaplastic carcinoma.

We present a case of malignant melanoma of the rectum with four photographs. The patient has been followed from May 14, 1939 to the time of her death, March 9, 1941.

CASE REPORT

S. P., a female, aged forty-nine, was admitted May 14, 1939 to Coney Island Hospital, and discharged May 28, 1939. She had a protruding mass from the rectum.

During the past two years the patient had been troubled with a protruding mass from her rectum following each bowel movement. At first the mass was small and reduced itself spontaneously. During the past eight months it had become larger and more difficult to reduce. Patient moved her bowels six to seven times daily, a small amount at each movement. There was no watery diarrhea. The stools were normal in contour and brown in color. Tenesmus was present at each bowel movement and there was bleeding at times with stool.

On rectal inspection there was slight eversion of the anal mucosa on straining. One small hemorrhoid was seen. One could feel a lemon-size, nodular, pedunculated mass, whose stem was thin and close to the anus. The mass arose from this stem and was in the rectum. It was nodular and hard. On the right side of the mass was a similar one, about the size of a small nut, arising from a small band above the anus.

Impression: Anal polyp-external hemorrhoid.

The patient was operated upon May 15, 1939.

The specimen consisted of two irregular masses, the larger measuring 3 by 2 by 2 cm., pinkish in color and nodular in outline. On section the mass was homogenously grayish-white.

Microscopically, the sections were covered in one area with stratified squamous epithelium, showing transition to columnar epithelium. (Figs. 1 and 2.) The entire stroma was the site of a dense, neoplastic infiltrative process consisting of single cells, groups of cells and irregular acini. The cells showed a marked variability in size and shape of the nuclei. Innumerable mitotic figures were present. The entire process was one of immaturity.

Diagnosis: Anaplastic carcinoma of the rectum.

The patient refused radical surgery and was referred on May 28, 1939 to the Brooklyn Cancer Institute, at the Kings County Hospital, Brooklyn, New York.

At the Brooklyn Cancer Institute, where we saw the patient the history was as follows:

The patient, S. P., a female, aged forty-nine, was admitted June 6, 1939 and discharged July 7, 1939 with a complaint of rectal tenesmus.

On palpation a small, pea-sized nodule was felt just above the sphincter on the posterior wall. This appeared to be an inflammatory thickening. Proctoscopic examination revealed what appeared to be an inflammatory mass on the posterior wall about 1 cm. in diameter, with a dark bluish mass just above. The patient, however, refused operation and signed her release July 7, 1939. During the interval the patient received deep *x*-ray therapy. The patient was admitted a second time on September 20, 1939 complaining of severe rectal tenesmus. Examination at this time showed that the mass was now about 1½ cm. in diameter and the bluish mass just above had increased in size. The patient was taken to the operating room for removal of the growth for biopsy and the insertion of radon seeds. The pathologic report was as follows:

The rectal mucosa was intact, one portion undergoing compression atrophy, due to the presence in the submucosa of multiple, large, fairly discrete masses of atypical cells. (Figs. 3 and 4.) The majority of these were in no definite arrangement. An occasional group tended to form a pseudogland. The individual cells were large, with poorly defined cell boundaries, a pale pink or foamy cytoplasm and nuclei which vary considerably in appearance. The majority were vesicular, round or ovoid, with small basophile nuclei. Others were hyperchromatic and irregular, with occasional regular mitotic figures. In some areas both in the stroma and within the tumor cells were collections of granular brown pigment which did not take the stain for iron. There was a little fibrous reaction and a scant infiltrate of lymphocytes. Diagnosis: Malignant melanoma.

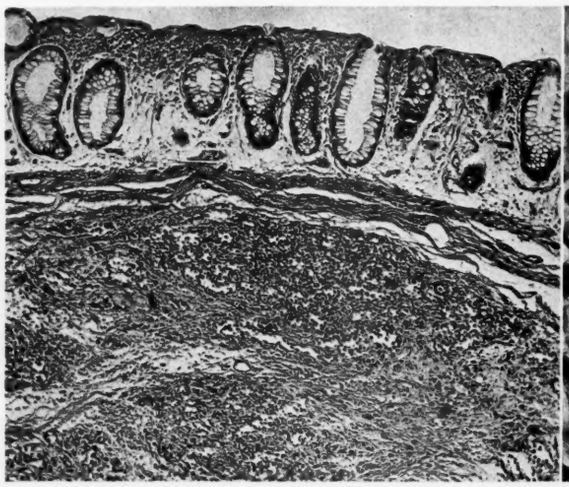

Fig. 3. Study of section of mass removed September 20, 1939. Rectal mucosa is intact. In the submucosa are seen multiple, large, fairly discrete masses of atypical cells; there is occasional pseudogland formation (low power).

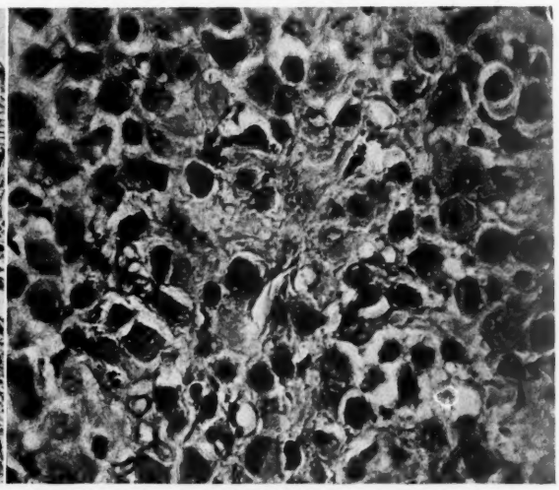

Fig. 4. Study of section of mass removed September 20, 1939. The individual cells are large, with poorly defined boundaries. The majority are vesicular, round or ovoid, with basophilic nuclei. Others show hyperchromaticity, anaplasticity and mitosis. In some areas, collections of granular, brown pigment which do not take the stain for iron are seen located in either the stroma or tumor cells. Fibrous reaction and lymphocytic infiltration are slight (high power). Diagnosis: malignant melanoma.

At the patient's insistence and her refusal of further treatment she was discharged on September 25, 1939, and referred to the outpatient department. On October 5, 1939 there were numerous pigmented spots on the left arm, left side of the neck and on the left wrist. The patient refused all further treatment.

The patient got along fairly well at home for almost one year, when she began to complain of weakness in her legs and for several weeks inability to walk. She was readmitted to the hospital for the third time on November 14, 1940, when examination showed for the first time enlargement of the inguinal lymph-nodes. One of the lymph-nodes was removed for biopsy with the following report:

Small areas of lymphoid tissue still remained. The remainder of the node was completely replaced by tremendous sheets of atypical cells, closely crowded, but tending to have an alveolar arrangement. The individual cells were large, many were round, or polyhedral in outline, with distinct cell boundaries; others appeared inter-

connected by fine processes. The cytoplasm was pale pink, the nuclei varied considerably in size, shape and staining capacity. They were either vesicular or hyperchromatic and irregular, and had occasional multinucleated cells. There were scattered regular mitotic figures. Fibrous reaction was minimal. No pigment was present.

Diagnosis: Metastatic melanoma (rectal origin).

X-ray examination showed the following: On November 25, 1940 there was no evidence of bone metastasis to the spine. Chest plate showed a supracardiac shadow, from which a soft tissue mass bulged into the left lung field for about one inch. The mass had a well-defined, irregular wavy outline. On December 2, 1940, the right foot showed rarefying metastasis of plum-pit size within the base of the fifth metatarsal and the third metatarsal bones. A pathologic fracture was noted in the third metatarsal, and there was a rarefying metastasis in the posterior aspect of the fibula two inches above the lower end. On December 3, 1940 a rarefying metastasis in the left ring finger, right metacarpal bone, left foot third metatarsal and metastasis in both femurs was noted. On December 11, 1940, numerous rarefying metastasis about 1 cm. in diameter was seen in the lateral skull. On January 31, 1941, a pathologic fracture of the right femur occurred and involvement of the right half of the pelvis was noted.

The patient expired in the hospital on March 9, 1941. We are embarassed in not having the autopsy findings, but at the time the patient expired four of the resident surgeons left the hospital to enter the Army. We were not notified that the patient had expired until the following day, when we found that the body had been removed without a request for an autopsy, which we are certain would have been granted.

SUMMARY

1. The origin and significance of melanin in malignant tumors is reviewed.

2. Melanomas of the intestinal tract constitute 2 to 3 per cent of all melanomas and are most frequently found in the rectum.

3. A case of malignant melanoma of the rectum is reported.

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TUBERCULOSIS OF THE THYROID GLAND WITH HYPERTHYROIDISM*

CASE REPORT

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TUBERCULOSIS of the thyroid gland is rarely evident clinically. There are two types of the surgical forms of this disease reported: One assumes a clinically symptomless course or is associated with hyperthyroidism; the other consists of the cases of chronic tuberculosis of the thyroid gland in which great numbers of isolated nodules increase in extent, or the gland enlarges through caseation and abscess formation. Under the latter circumstances, symptoms supervene which differ from the usual goiter symptoms and are variably interpreted. The latter frequently suggest malignancy, Riedel's struma, etc. Rarely are they diagnosed as tuberculosis.

The case about to be reported, belongs to the first group, that is, tuberculosis of the thyroid gland associated with Basedow's disease. This clinical entity has been previously described both clinically and histologically, and it is a generally accepted fact that tuberculosis is a cause of Basedow's disease, notwithstanding the claims of several investigators to the contrary.

The case about to be reported was free of any tuberculous manifestations and the course was so unusual and different, that a detailed review of the literature would be out of place here.

CASE REPORT

The patient, Mrs. D. M., was first seen June 14, 1938. Her present illness began four months previously with loss of appetite, vomiting and occasional diarrhea. The patient felt weak and tachycardia was present on slightest exertion or excitement. She slept well and had lost thirty-five pounds in five months.

Her pulse rate during this examination was 140, basal metabolic rate, plus 40; there was no dyspnea, cough, or melena.

The patient was put on Lugol's solution m-x and phenobarbital gr.ss three times a day and was told to rest. Later, June 26, 1938, she was admitted to the Beth Israel Hospital. The history given by the patient at that time was essentially the same, except that her pulse had slowed down considerably. The physical examination showed a fairly well nourished, white female, forty-three years old. She was sixty-one inches tall and weighed 129 pounds.

There was a slight exophthalmos, no lid lag, the pupils were normal, and the throat was not injected. There were no palpable lymph glands. There was a suprasternal mass in the midline and right side which moved up and down on swallowing.

The chest and lungs were negative to percussion and ausculation. The heart sounds were of good quality, sharp and accentuated. Blood pressure was 120/80. The abdomen was negative for any pathological finding. There was a slight tremor of the right upper extremity. The basal metabolic rate taken June 29, 1938, was plus 28. *X*-ray picture of the neck and chest was entirely negative.

Blood Count: Red cells—4,300,000
White cells—7,700
Polynuclears—76%
Hemoglobin—86%

Blood Chemistry: Wassermann—negative; Kline—negative.
Urea nitrogen, 28.
Cholesterol, 375.
Cholesterol esters, 150.
Sugar, 88.

* From the Surgical Service, Newark Beth Israel Hospital.

A blood iodine determination was not done. The vocal cords were normal.

The patient was sent to bed and Lugol's solution and phenobarbital were continued. She continued to respond well, and gained five pounds in eight days. The pulse showed a steady rate between 80 to 90.

A subtotal thyroidectomy was performed on July 5, 1938. A bilateral multiple adenoma containing numerous white nodules, some calcified, was removed. The pathological report of the specimen was as follows:

Gross Examination. The specimen consisted of two lobes of thyroid tissue together with the isthmus. They measured 4 by 3 by 1½ cm., 4 by 2½ by 2 cm. and 2 by 1 by 1 cm. The surface of each portion was smooth and intact, except at the point of resection. The tissue was moderately firm in consistency and, on section, was composed of brownish-red and reddish, fleshy-appearing tissue. In addition, there were numerous well defined cystic structures, varying from 1 to 1½ cm. in diameter. These were, for the most part, surrounded by a thick wall of greyish and greyish-yellow fibrous-appearing tissue and were filled with reddish, yellowish-red and brownish, soft, almost friable tissue. Still other cystic structures which were present were smaller, being from 2 to 3 or 4 mm. in diameter, and were filled with a gelatinous greyish material.

Microscopic Examination. The thyroid follicles varied greatly in size. The majority were lined by cuboidal epithelium which enclosed the homogeneous eosinophilic colloid. There were occasional greatly enlarged follicles, lined by a thick wall of fibrous tissue and an inner lining of flat cubodial epithelium filled with colloid and red blood cells. Distributed irregularly throughout the section were thick cords and thinner strands of fibrous tissue distinctly separating follicles from each other in some areas and encapsulating groups of follicles in others. Collections of round cells were found within the fibrous strands, as well as areas of hyalinization and calcification. An occasional granulomatous area was found consisting of necrotic débris in the center, surrounded by epithelioid cells, giant cells and round cells, the latter being more numerous at the periphery areas. No acid-fast bacilli were found in the granulomatous nodules.

The postoperative course was uneventful except for a moderate degree of hoarseness.

Laryngoscopic examination showed both vocal cords in central position and fixed. It was feared that this might be a permanent condition due to possible nerve injury, however, the right cord recovered about five days after the operation. Examination on October 12, 1938, in the out-patient clinic showed complete recovery.

The patient was allowed out of bed on July 12, (eight days postoperatively), but as a precautionary measure was not allowed to leave the hospital until July 24, (twenty days postoperatively). The wound was entirely healed at this time and the patient gained 8 pounds in weight.

On August 28, 1938, she presented herself to Dr. Rados, complaining of pain and redness of her right eye. An ophthalmogical report follows:

The patient was first seen on August 28, 1938. She complained of painfulness and redness of her right eye for the past three weeks. One month previously, thyroid operation was performed by Dr. Comando.

Vision in the right eye was 15/20, in the left eye, 15/20. The right eye showed marked ciliary congestion, numerous small white deposits on the lower part of the Descemet membrane. The right pupil was much smaller than the left and the fundus was not clearly visible; the left fundus was normal.

Diagnosis: Acute iridocyclitis of the right eye.

Wassermann and Kline tests were negative; the Mantoux test was strongly positive after twenty-four hours.

On September 9, the patient showed marked deep infiltration of the posterior layers of the cornea. The infiltration was spotty in type, the iris hyperemic; at the pupillary margin, at 12 o'clock, 6 o'clock and 7 o'clock, small grayish vascularized nodules were present. Ciliary congestion increased and the eye was very painful.

Diagnosis: Keratoiritis and tuberculums of the iris in the right eye.

Tuberculin treatment was instituted and has worked very satisfactorily.

On January 19, 1939, the ciliary congestion had cleared up and the eye was white and painless. There were numerous, small, deep-seated corneal opacities corresponding to the previous sites of the infiltrates, the tuberculums of the

iris had gradually been absorbed, the pupil was dilated to maximum and there were no inflammatory symptoms in the iris and the ciliary body.

The clinical findings and the prompt response to the administration of tuberculin indicate the tuberculous nature of the lesion.

SUMMARY

The unusual features of this case are:

1. A bilateral nodular toxic goiter with areas of calcification, etc., was present.

2. No primary tuberculous lesion elsewhere in the body was demonstrated.

3. Tuberculosis of the eye followed about five weeks after the thyroidectomy. This was undoubtedly metastatic and was probably brought about by the operation.

4. There was complete recovery of the eye following treatment with old tuberculin and the patient was in perfect health six months after the operation. The eye healed completely, 35 pounds in weight were gained, and the basal metabolic rate was plus 4.

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ANEURYSM OF THE HEPATIC ARTERY*

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THE object of this paper is to report a case of aneurysm of the hepatic artery and to discuss the subject in the light of the information available.

CASE REPORT

A housewife, fifty-two years old, was brought to Freedmen's Hospital on December 8, 1940, in severe collapse. Her daughter related that about one month earlier the patient had complained of severe abdominal pain, following a heavy meal and that for a few days thereafter tarry stools were passed. Four days prior to admission she suffered a second attack, following a heavy meal, which was characterized by persistent epigastric pain, hematemesis, later melena and eventually "shock."

The patient was of normal development, well nourished and presented the following salient findings: restlessness in spite of evidences of severe collapse; blood pressure 60/40; icteric sclera; pale mucous membranes; natural but rapid and somewhat faint heart sounds; natural lung fields; soft abdomen, though tender above the umbilicus; liver, spleen or abnormal masses not palpable.

The erythrocyte count was 1,940,000; hemoglobin 42 per cent; leucocyte count 16,780. The urine was not examined: the patient did not void while in the hospital and she was not catheterized.

Because of the history and clinical evidences of hemorrhage, immediately after admission the patient was given by vein 300 cc. of whole blood followed by 3,500 cc. of 5 per cent glucose in normal salt solution. Shortly thereafter, the patient had a severe hematemesis amounting to about 450 cc. In spite of the administration of additional fluids, the patient failed to improve and expired at 11:00 A.M., December 9, 1940, slightly over fourteen hours after admission.

The significant external findings two hours after death were pallor and unclotted blood in the oral cavity and rectum. There was no free fluid in the abdominal cavity, but the stomach, cecum and ascending colon were distended with clotted and unclotted blood, amounting to 1,365 cc. in the stomach and 950 cc. in the proximal colon. In the duodenum, 3.5 cm. from the pyloric sphincter, there was a bleeding ulcer .5 by 7 mm. in size and within 1.5 cm. distally there were two nonbleeding ulcers 3 and 4 mm. in diameter. These ulcers occupied a dark purple and softened oval area 3 by 5 cm. in diameter, located about the center of a swelling 4.5 by 9 cm. in size, involving most of the posterior wall of the first and second parts of the duodenum. These lesions were in relation to a large, partially hemorrhagic and firm mass, with foci of softening, found behind the duodenum and extending in the gastrohepatic ligament from the pancreas to the hilum of the liver. The liver was normal, but the gallbladder was compressed slightly on the medial side; the extrahepatic bile ducts and the portal vein were displaced backward and slightly to the right and were compressed; the foramen of Winslow was obliterated; the head of the pancreas was the seat of hemorrhage and the duodenal wall was necrotic in relation to parts of the hematoma. This mass had resulted from an aneurysmal dilatation of the hepatic artery 2 cm. from its origin and a perforation in relation to the head of the pancreas and duodenum, producing a hematoma. The preserved parts of the intima within the aneurysm showed wrinkling together with calcification in areas of atherosclerosis. The walls had a lobulated contour; the lumen was filled with a laminated thrombus. (Fig. 1.) The left branch of the hapatic artery was found coursing upward to the liver from the superior surface of the aneurysm at a point about 4.5 cm. from the latter's proximal end. The right branch was traced from the liver to the superior surface of the aneurysm, about 1.5 cm. to the right of the origin of the left branch, but no opening into the aneurysm was found at this site.

The circulatory system showed in addition to the lesions of the hepatic artery, moderate hypertrophy of the left ventricle of the heart

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and mild atherosclerosis of the aorta and its main branches. The respiratory system revealed slight aspiration of blood into the larger

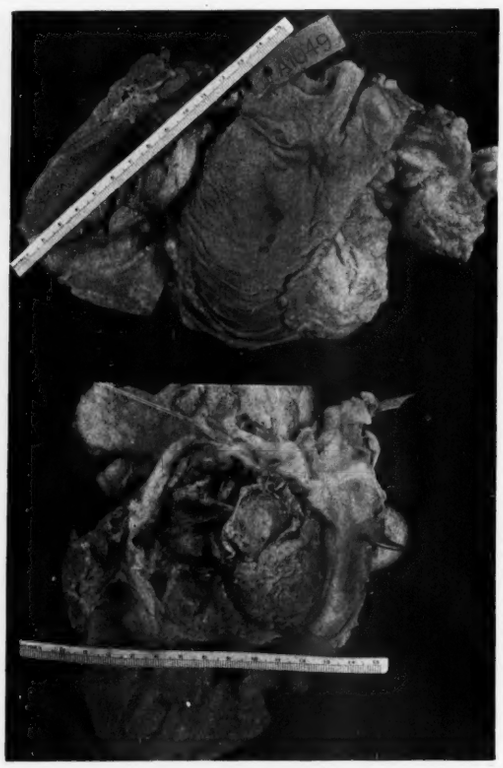

Fig. 1. Aneurysm of the hepatic artery. Above, the duodenum overlies the aneurysmal mass. Below, the duodenum is displaced to the right and the hepatic artery is indicated by the double thread in the upper part of the photograph.

bronchi. The other gross findings were not significant.

Microscopically, there were no recognizable syphilitic lesions of the aorta. The intima showed early atherosclerosis and the media widespread areas of degeneration, showing basophilic staining. A longitudinal section extending from the hepatic artery into the aneurysmal sac revealed a nearly normal arterial wall, thickened by fibrosis of the adventitia and slight intimal atherosclerosis, which changed gradually, showing irregularly progressive thickening of the intima by atherosclerosis with focal calcification over a thinning media and a progressively thicker adventitia. (Fig. 2.) Similar but more severe intimal changes were found in other sections of the aneurysm where the media was replaced in large measure by fibrous tissue in the form of scars which united in places the fibrous tissue of the intima with the thickened adventitia. Overlying the intima were thrombi, showing layers of varying ages. The thickened adventitia was the seat of leucocytic infiltration, consisting of lymphocytes, plasma cells and

Fig. 2. Longitudinal section of the proximal part of the aneurysm.

monocytes, aggregated particularly about blood vessels but the latter did not show obliterative intimal proliferation. (Fig. 3.) Focal collections of similar cells with small capillaries forming granulation tissue were found focally where the media was severely compromised and in places this type of tissue with some collagenous deposits was the entire aneurysmal wall. Toward the duodenum the vascularized scar tissue which constituted the aneurysmal sac gave way so that blood clots were adjacent to the muscle coats. This rupture appeared to have been recent, for well preserved erythrocytes were identified in the clot and there was very little leucocytic infiltration of the duodenal wall at this site.

In the liver there was a widespread and severe microphage infiltration of the sinusoids with degeneration of the cord cells and occasional foci of necrosis. In the kidneys there was slight arteriosclerosis with an occasional cortical scar bearing hyalinized glomeruli. In the other organs the changes were not significant aside from slight edema of the lungs.

DISCUSSION

Incidence. Aneurysms of the hepatic artery are among the rarer types of vascular lesions. The latest comprehensive report made in English appeared in 1923 when Friedenwald and Tennebaum[3] added a case to the sixty-four they had been able to find recorded up to that time. We have found nineteen additional reports, which with our own, brings to eighty-five the number of cases now on record.[1–2,4–20]

Sex. The condition is found in a 3:1 ratio in males and females, for of the eighty-

two cases in which sex was recorded, sixty-two were males and twenty females.

Age. The age distribution is wide: the youngest case being a boy ten years old and the oldest a man of eighty-three years. The average for the entire group was thirty-eight years; for males thirty-six years and for females forty-two years.

Table 1

ETIOLOGY OF ANEURYSMS OF THE HEPATIC ARTERY

Infections		41
With Inflammation at the Aneurysmal Site		16
Syphilis	7	
Cholecystitis	4	
Liver Abscess	2	
Peri-arteritis	2	
Tuberculosis	1	
Likely to Produce Inflammation at the Aneurysmal Site		21
Pneumonia	7	
Osteomyelitis	4	
Bacterial endocarditis	3	
Embolism—source not stated	2	
Typhoid fever	2	
Influenza	1	
Phlegmon of leg	1	
Suppurative mediastinitis	1	
Not Likely to Produce Inflammation at the Aneurysmal Site		3
Pleurisy	1	
Pulmonary tuberculosis	1	
Type of infection not stated	1	
Arteriosclerosis		15
Trauma		7
Cholelithiasis		5
Diagnosis not stated		17
Total		85

Etiology. The causes of the condition are varied but infectious processes appear to be the most important group, accounting for forty-one or 60 per cent of the sixty-eight cases in which the cause was given. Next in order of frequency are arteriosclerosis with fifteen cases (22 per cent) and trauma with seven cases (10 per cent). The infectious processes reported vary from those which appear to have been the causes of aneurysms to those in which this relationship appears improbable. (Table 1.) It is of interest that syphilis, which is the most common cause of aneurysms of large arteries, ranks well below arteriosclerosis with only six cases in which it appeared to have been the cause and one doubtful case. Though cholelithiasis has been reported as a cause in five cases, we are of the opinion with Tenani[18] that the concomitant cholangitis is perhaps a more important factor than the pressure afforded by the concretions. It is conceivable that in cases wherein the lesion encroaches upon a passage of the digestive system, the intake of food and the normal processes of digestion may, as in our case, be a factor in precipitating hemorrhage.

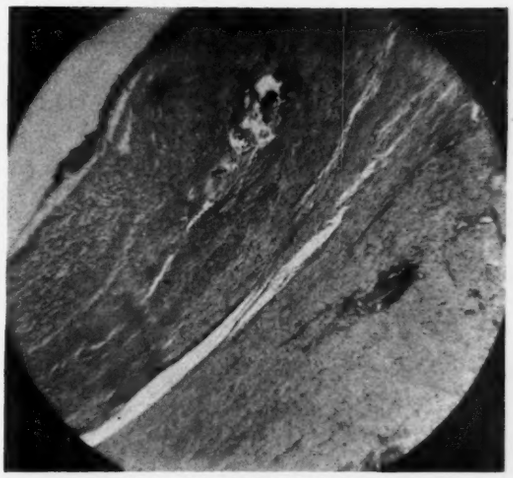

Fig. 3. Higher magnification of the part of the aneurysmal wall indicated by the India ink dot in Figure 2. The intima is thickened by aerosclerosis with a focus of calcification and is overlaid in part by a thrombus; the media shows a defect beneath the point of calcification; the adventitia is thickened by scarring, and its perivascular lymphocytic and plasma cell infiltration is not associated with obliterative endarteritis.

Pathology. Grossly, the most important features about aneurysms of the hepatic artery are their position, number, size and relationship to adjacent structures. Based upon their position, either within or without the liver, these aneurysms have been subdivided into two groups: the intrahepatic and extrahepatic. The latter is by far the larger group for of the eighty-four case reports in which the positions of the aneurysms were recorded, sixty-one subjects had them outside of the liver; twenty had them within the liver and three subjects had both intra- and extrahepatic aneurysms. Based upon the artery of origin, the distribution was: hepatic artery–forty; right branch–twenty-six; left branch–seven; both right and left branches –one; cystic artery–three and gastroduodenal artery–one.

These aneurysms are usually single, though the following instances of multiple aneurysms have been reported: two aneurysms in each of six cases; three in three cases; four in one case; five in one case and "several" in one case.

The aneurysmal sacs vary from the size of barleycorn as found by Rolland to that of a child's head, as found by Wallmann.[3] The extrahepatic sacs are usually larger than the intrahepatic ones, though the largest intrahepatic aneurysm recorded, that of Pugliatti,[14] was about the size of a full-term fetal head.

The smaller aneurysms of the hepatic artery are usually true aneurysms, resulting from a dilatation of the vascular wall; the larger ones, however, are in part false aneurysms or hematomas, resulting from the rupture of the weakened vascular wall into the retroperitoneal tissues. Both the true and false aneurysms become adherent to surrounding structures by fibrous adhesions of varying density and may cause compression, particularly of the bile ducts. Eventually, most of the aneurysms rupture either into the abdominal cavity, which is true in most instances, or into some adjacent structure. Rupture occurred in sixty-seven of the eighty-five cases reported to date. Of this number thirty-one ruptured into the abdominal cavity; twenty-two into the extrahepatic bile ducts; seven into the duodenum; six into the gallbladder; one into the stomach and one into the portal vein. In four subjects there were double ruptures: in two rupture occurred into the duodenum and abdominal cavity; in one into the gallbladder and abdominal cavity and in one into the hepatic and common bile ducts. Of special interest are the reports of two subjects[3] who had exhibited clinically hemorrhage into the gastrointestinal passages though at necropsy no perforation of their intrahepatic aneurysms was found. We believe that in these cases and perhaps in others, a rupture occurred into intrahepatic bile ducts.

Microscopically, in addition to the evidences of recent and remote hemorrhage and thrombosis, there are evidences of inflammation and less frequently of arteriosclerosis. In the vessel wall the inflammatory reaction is commonly in keeping with a traumatic or bacterial origin but only rarely syphilitic. Atherosclerotic changes with calcification, of sufficient degree to be considered of etiologic importance, are found in nearly a fourth of the cases. In all aneurysms, but particularly in the older ones, there is evidence of healing which ranges from granulation tissue growth into the sites of hemorrhage and thrombosis to dense collagenous scarring.

Symptoms and Signs. The symptoms and signs of aneurysms of the hepatic artery are varied, but there are three which occur with sufficient frequency to warrant considering them specially as aids in diagnosis. These are: pain, hemorrhage and jaundice. Pain is by far the most common of these, occurring in fifty-eight cases. It is usually felt in the right hypochondrium or in the epigastrium or both; it varies in intensity from a feeling of pressure to severe colicky pains; it may be intermittent or constant and its onset may be precipitated by a known factor or without apparent cause.

Next in frequency is hemorrhage which occurred in forty instances. It is usually profuse and in the form of hematemesis or melena, though occasionally it is detected merely as occult blood in the stools and in some instances repeated small hemorrhages produce secondary anemia. Whenever hemorrhage is apparent externally, the aneurysm has ruptured either directly into the digestive passages or indirectly through the biliary ducts, but cases of hemorrhage into the liver or into the abdominal cavity may not be recognized except by the signs and symptoms of internal bleeding. When pain and hemorrhage occur in the same patient, hemorrhage usually follows pain.

Jaundice is the least frequent of the three most common symptoms and signs, occurring in thirty-six cases. It is usually of the obstructive type and is caused by compression of the common duct by the aneurysmal sac or by rupture of the aneurysm into the

duct causing obstruction by a clot. In many cases the jaundice is intermittent, but it may be persistent and severe, accompanied by pruritus.

Less common symptoms are fever, noted particularly in those cases associated with infectious processes and also asthenia, headaches, constipation and ascites. A pulsating tumor with a systolic murmur and enlargement of the liver are considered by Lambert and Secretan[6] and by Bickhardt and Shumann[3] as important signs.

Duration. The duration of the condition from the time of onset of symptoms or signs to the diagnosis, varies from a few hours to several months, with an average of about four or five months.

Diagnosis. Largely because of the rarity of aneurysms of the hepatic artery, their diagnosis is seldom made, having been made before death or operation in only two cases, though there are instances wherein the diagnosis was made at operation. It would seem, however, that having the condition in mind, the diagnosis should not be difficult in a subject exhibiting epigastric or right hypochondrial pain, hemorrhage and juandice, particularly so when the process accompanies or follows a generalized infection. If the patient should present in addition a pulsating abdominal tumor with a systolic murmur and enlargement of the liver, the diagnosis of aneurysm of the hepatic artery should be relatively easy. In arriving at a diagnosis the more common pathological processes affecting the tissues and organs of the right upper quadrant of the abdomen and lower chest must be considered and ruled out.

Treatment. The treatment of aneurysms of the hepatic artery, like that of aneurysms in general, is unsatisfactory. Ligation, the only form of therapy employed to date, is dangerous because it is likely to result in death from liver necrosis or insufficiency. Yet, the facts that there are recorded two instances of recovery after operation and that some cases recover spontaneously, offer the hope that if the diagnosis were made, the surgical approach, (perhaps by gradual reduction of the blood supply to the part and the establishment of a collateral circulation) might lead to a larger per cent of cures. At present, however, the prognosis is decidedly unfavorable.

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PERFORATED PEPTIC ULCER COMPLICATED BY ACUTE PURULENT APPENDICITIS*

CASE REPORT

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THAT a patient having a peptic ulcer may also harbor chronic appendicitis is a well known fact. However, the incidence of a perforated peptic ulcer complicated by acute appendicitis is very rare. This is borne out by the fact that in the medical literature for the last fifteen years, only nine such cases have been reported. Of these, eight were found in the French, Italian, Russian and Spanish medical literature and one in the English.

In addition, a case that suggested the co-existence of the two conditions was reported in 1911 by Andre.[2] An appendectomy was performed on a woman presenting the signs and symptoms of acute appendicitis. During convalescence she developed a cough with purulent expectoration. Cultures of the sputum showed streptococci, staphylococci, and Koch bacilli. The patient died and the autopsy revealed a subdiaphragmatic abscess connected with a fistula to a perforated round ulcer of the pyloric portion of the duodenum. The perforation is supposed to have occurred after the appendectomy.

Another case in point that borders closely on the type of cases discussed in this paper is that reported by R. W. John.[13] A boy six years old was operated upon for acute suppurative appendicitis. Six days after the operation he died of hemorrhage. At autopsy "a perforating ulcer was found on the posterior wall of the duodenum, which penetrated the entire gut and eroded the gastro-duodenal artery and caused the fatal hemorrhage."

CASE REPORT

C. T., age twenty-three, a male factory employee, was well when he went to bed at 1 A.M. on August 31, 1941. Before retiring he drank a bottle of carbonated water. At 5 A.M. a sudden stabbing pain in the abdomen awakened him. He vomited shortly afterward. The pain was continuous and was accompanied by pain in the left shoulder. One and one-half hours later I found him sitting up in bed in a doubled-up position with his hands over the abdomen pressing against the epigastrium and umbilical region.

Four years ago he had severe cramps in the abdomen which kept him from work for three or four days. Another spell of cramps lasting one day occurred two weeks previous to the present illness. Otherwise, the patient had never had any gastrointestinal symptoms, such as, hunger pain, after meal distress, heartburn, etc.

Examination revealed a well nourished adult male in severe pain. Pulse and temperature were normal. There was marked board-like generalized rigidity of the abdominal muscles with maximum tenderness in the region of the umbilicus and to the right of this area. Liver dullness was not obliterated. His blood count showed 10,200 white blood cells, 70 per cent polymorphonuclears, 10 of which were nonfilamentous. Urine examination was negative. A preoperative diagnosis of an acute condition of the abdomen with ruptured abdominal viscus was made.

Three hours after onset of symptoms operation was performed under spinal anesthesia. A right midrectus incision was made and the abdomen was opened in layers. On opening the peritoneal cavity there was a considerable

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amount of exudate covering the loops of the small bowel. Dark brown fluid was found in the right iliac fossa and seemed to be welling up from the pelvis. The appendix was found covered with the exudate, distended at its distal half and injected, but no perforation was noted. The meso-appendix was short and thick. Adhesions bound the appendix to the cecum. The ileum was explored for about thirty inches from the ileocecal junction and no diverticulum was found. As the pathological condition found in the appendix was not sufficient to account for the extensive exudative peritonitis, the incision was extended to the epigastrium. The gallbladder had its normal bluish color except that in places it was covered with the same exudate. The latter also covered the serous surface of the liver. However, in the pyloric region on the anterior surface of the stomach a punched-out opening was found about 2 cm. from the border of the greater curvature. The opening was about ½ cm. in diameter. The stomach wall surrounding it was moderately indurated.

Appendectomy was performed. Two guy sutures were placed at the greater curvature on either side of the perforated ulcer. An intestinal purse-string suture was used to close the opening. This was reinforced by a row of mattress sutures placed in the transverse diameter of the stomach. The end of the omentum was then anchored over the line of sutures. A cigarette drain was placed at the pyloroplasty and brought out through the upper apex of the incision. A similar drain was inserted in the pelvis and brought out through a stab wound in the right lower quadrant. Five Gm. of sulfanilamide were placed in the peritoneal cavity. The abdomen was closed in layers.

There was a distended appendix 5 × 1 cm. The wall appeared edematous and the lumen contained blood. There was diffuse exudative infiltration of the appendiceal wall. (Fig. 1.)

Microscopic diagnosis: Acute purulent appendicitis.

Wangansteen suction was begun immediately after the operation and continued for five days. After a slightly elevated temperature for the first four days, it became normal and stayed so throughout the rest of the convalescence. The pulse and respirations were normal throughout. The drains were removed on the seventh postoperative day. The patient was discharged from the hospital on the sixteenth day with the wound healed by first intention.

In studying the reports of the other nine cases, few striking findings were encountered. All cases reported, with the exception of Andre's[2] case, occurred in males. The age of the youngest patient was fourteen years, and the oldest was sixty-seven years.

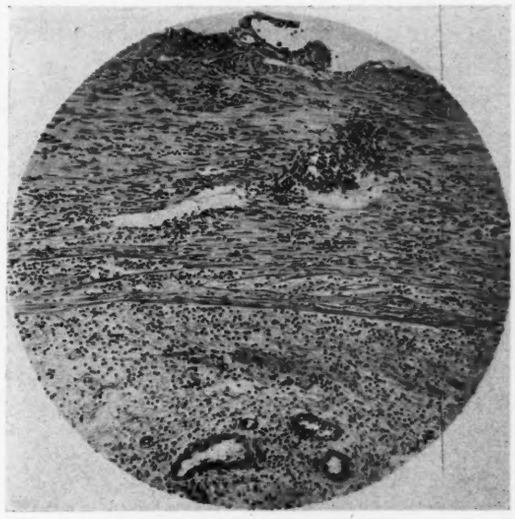

Fig. 1. Diffuse exudative infiltration of appendiceal wall.

In the history of these patients we find that four of them, with the exception of having very short and rare spells of indigestion or cramps, did not have any signs and symptons of peptic ulcer. During the acute attack most of the patients were known to have vomited once, while the nausea continued, so that one is justified in concluding that the stomach was emptying itself intraperitoneally. The location of the pain in all of the cases reported was chiefly in two areas: the epigastrium and the right lower quadrant or the right periumbilical region. However, in three cases the pain was found only in the right lower quadrant.

The preoperative diagnosis in practically all of the cases was acute appendicitis with or without peritonitis.

The anesthetic used was spinal in two cases and general in five. In four reports the type of anesthesia was not mentioned. With the exception of one case, the procedure was appendectomy, extension of the incision to the epigastrium, and simple

closure of the perforation with a tag of omentum anchored to it. In Scalfi's[19] case a posterior gastroenterostomy was carried out in addition to the closure of the perforation.

There were six anterior prepyloric perforations and four perforations of the duodenum. In one case of Pascali and Rodriguez-Ramos[16] the perforated ulcer occupied part of the pylorus and part of the duodenum. All but one of the cases reported, including the author's were drained.

During the period of convalescence, two cases developed complications. Serra's[20] case showed a rise in temperature and pulse and leucocytosis on the seventh postoperative day. The only finding was a positive Widal in 1:40 and 1:80 dilution (typhoid fever). Under appropriate measures (quinine and neoprontosil), the patient recovered and left the hospital cured. In the other case, reported by Scalfi,[19] in which a gastroenterostomy was performed in addition to the closure, the patient developed pneumonia and was taken home by his relatives in a moribund condition.

That peptic ulcer is a much more common disease than is clinically diagnosed is proved by autopsy statistics. Portis and Jaffee[17] (1938) report the finding of 457 cases of peptic lesions in 9,171 autopsies performed between June 1, 1929, and December 31, 1936, a total incidence of about 5 per cent. In these 457 cases, peptic ulcer was the essential lesion in 118, and in 221 it was the incidental lesion. They also found that when peptic ulcer was the essential lesion the duodenal localization predominated. In studying the incidence of perforation of peptic ulcers in North America, Brown[5] found that about 5 per cent of the ulcers perforate acutely, while chronic or subacute perforating ulcers constitute 25 per cent of cases of ulcer. In a series of 33,439 cases of gastroduodenal ulcers collected from the literature, DeBakey[6] found that there were 4,410 (13.2 per cent) cases of perforation. In a detailed study of 500 cases in 1937, Thompson[22] reported that acute perforated peptic ulcer occurred predominately in the male (94.2 per cent).

The question arises in this series of cases: Which of the two conditions was primary, the appendicitis or the perforated ulcer? In support of the assumption that the patient had a peptic ulcer without the signs and symptoms thereof long before the development of acute appendicitis, we find a statement by Steward[12] who believes that the process of peptic ulceration from the onset to the time of complete perforation of the muscular coat occupies at least two months.

On the other hand, Mahmert,[14] as early as 1907, was the first to render evidence that inflammation of the appendix plays an important rôle in producing certain peptic ulcers. Pascalis and Rodriguez-Ramos,[16] from observation as well as experimental studies on dogs, conclude that an ulcer once found in the pyloric region gives rise to the inflammation of the appendix either through the peritoneal route, i.e., by contact, or through the lymphatics, or the infected material from the peptic ulcer reaches the lumen of the appendix through the digestive tract.

Among those who believe that the reverse is true, namely, that it is the presence of appendicitis that gives rise to the formation of peptic ulcer, we find M. P. Brodin and Mme. Tedesco.[4] They prove their contention by the distribution of the lymphatics: "The lymphatics of the appendix, ileum, and the cecum cross the third portion of the duodenum and, at the same time, the messenteric vessels. The inflammation of these lymphatics provokes a spasm and to a greater degree a compression of the duodenum with the arrest of food at that level, and the appearance of duodenal stasis with dilatation of its inferior portion. This stasis alters profoundly the duodenal function by favoring infection and modifying the normal chemistry of the chime at this important crossroad. The result of this mechanical infection and chemical alteration is an ulcer."

There seems to be more or less agreement as to the mechanism of perforation of the peptic ulcer in the presence of an acutely inflamed appendix. According to Almgovzen,[1] Scalfi,[19] Pascalis and Rodriguez-Ramos,[16] and Girand[10] the perforation is due to the spasm and active reverse peristalsis which is associated with acute appendicitis.

The pathological report, of course, was limited to the microscopic findings in the appendix and varied from that of acute appendicitis to that of gangrenous appendicitis.

In comparing the physical findings of this series of cases, one cannot select a definite set of signs and symptoms which would differ from the one we usually find in an episode of a ruptured abdominal viscus modified by the presence or absence of general peritonitis. However, we do find in the majority of the series reviewed that the pain of which the patients complained was in two areas of the abdomen, the right upper quadrant and the periumbilical region. In Flandin's[9] patient a roentgenologist diagnosed a "pathological appendix" two years before the last episode. But the patient was advised that "chronic appendicitis does not predispose to acute attacks. Therefore, no immediate operation is indicated."

In general, it may be said that the clinical signs and symptoms of an acute condition of the abdomen may be caused by a number of pathological conditions other than acute perforated ulcer alone or combined with acute appendicitis, but regardless of the underlying cause surgical intervention is imperative. In this regard Moynihan[15] put it quite aptly: "To make an anatomical and pathological diagnosis is a delight; to reach a decision that wherever and whatever the trouble the sooner measures of rescue are adopted, is a cardinal obligation." That the lapse of time between the perforation and the operation is one of the most important factors is emphasized by every author writing on this subject. Blackford and Baker[3] in an analysis of 933 cases of perforated peptic ulcer found that the mortality in the second twelve-hour period is double that of the first and that after the twenty-four-hour period it was more than four times as great. Harold L. Thompson[21] analyzes 500 cases of acutely perforated peptic ulcers. These were collected from the Los Angeles County General Hospital from September 9, 1921, to June 30, 1934. The operations were performed by fifty-seven surgeons. He concludes that "the gross mortality is around 40 per cent; that the mortality is lowest when operation is performed within six hours after perforation occurs, when the operation consists of suture of a tag of omentum over the closed perforation." This conclusion is well borne out by the mortality in this series. The only death occurring is the case in which a gastroenterostomy was done in addition to the simple closure and appendectomy.

On the other hand, in one of the patients of Pascalis and Rodriguez-Ramos[16] the perforated ulcers had penetrated into the pancreas. The adhesions were very dense. The surgeon closed the perforation without loosening the stomach from the mass of adhesions. On discharge the patient was advised to return for a gastric resection in the near future. Three months later the patient was symptom free. The roentgenologist reports "a freely movable, pliable stomach with normal peristaltic waves and no evidence of ulcer," thus pointing to a cure without further interference. The same was true of the other three cases in their series. Although some of them showed marked adhesions at the operation, they all recovered completely with normal anatomic and physiologic function. Graham[11] thinks that additional procedures are "meddelsome and unnecessary." Ross[18] reports the follow-up data of eighty-nine out of a personal series of 175 cases of perforated ulcer in which simple closure was used. The follow-up suggests that, provided the patient adheres to a strict diet for six months after operation and maintains dietetic care thereafter, his prospects

of cure are good. In a collected series of 1,525 cases of simple closure, DeBakey[7] reports that 65 per cent remained symptom free and 35 per cent continued to complain. Of the latter 16.9 per cent required subsequent operation. At this writing the author's patient (three and one-half months after the operation) has gained weight on a well balanced, ulcer-restricted diet, is free from symptoms, and continues his former gainful occupation.

CONCLUSIONS

1. A case of perforated peptic ulcer complicated by acute appendicitis is reported. Nine other such cases found in the literature are analyzed.

2. No age is exempt from being affected with acute appendicitis and perforating peptic ulcer.

3. A history of previous digestive disturbances is frequently missing.

4. The pain of which the patient complains is often located in two areas, the right upper quadrant and the right lower quadrant.

5. Liver dullness does not always disappear in perforating peptic ulcer.

6. The preoperative diagnosis in all the cases reviewed was acute appendicitis with or without preforation, and only postoperatively was the co-existence of the two lesions found.

7. The right rectus incision is the best suited for on acute condition of the abdomen with maximum tenderness in the right side. It allows, when indicated, an easier exploration of the abdominal contents.

8. When the pathological condition in the appendix is not sufficient to account for the extensive peritonitis present, it is imperative to search for another lesion in the abdomen, especially in the gastroduodenal region.

9. The wisdom of a long established rule, to operate whenever a diagnosis of appendicitis, acute or chronic, is made is reaffirmed by some of the cases in this series.

10. The mortality and results are best when the operation consists of appendectomy and simple closure of the perforation with a tag of omentum anchored to it. A number of these patients when re-examined months later were found symptom free with normal anatomic and physiologic function.

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BLASTOMYCOSIS OF CECUM*

CASE REPORT

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BLASTOMYCOSIS was described independently in 1894 by Gilchrist[1] and Busse.[2] The disease is caused by the blastomycete, a yeast-like organism which multiplies by budding in tissue but develops mycelial threads when growing in culture.

The part of the body usually infected is the skin where ulcerating lesions form. The disease may remain local or become systemic, invading the lungs, liver or gastrointestinal tract. Occasionally, it is primary in these organs. In addition to these sites, the organism has been found in the larynx, trachea, pleura, myocardium, spleen, pancreas, kidneys, adrenal glands, lymph-nodes, bones, joints, brain, spinal cord, urine, feces, sputum, blood, spinal fluid and prostatic secretion. The papers of Goto,[3] Hurley,[4] Stober,[5] Montgomery and Ormsby,[6] Powers,[7] and Wade and Bel,[8] are concerned with the various systemic manifestations of the disease.

An interesting observation is that the majority of the infections due to blastomycosis have been reported from the Chicago area. However, the disease has occurred in other states in the United States, South America, Canada, the British Isles, Continental Europe, India and Japan. Most of the patients have been males in the third decade of life and many of the American cases apparently showed a relationship to poor environment, hard work, and exposure, according to Sihler, Peppard, and Cox.[9]

Our patient was unusual in several respects. He had, as far as we were able to determine, no other lesion of blastomycosis except in the cecum. There was no skin infection, roentgenographic evidence of pulmonary involvement was lacking, and abdominal exploration at the time of operation revealed no other site in the gastrointestinal tract or abdominal viscera. Complete extirpation of the cecum and terminal ileum has apparently produced a cure. Finally, he was well above the average age of the other patients reported to have the disease.

The patient reported by Sihler, Peppard, and Cox[9] was found at postmortem examination to have blastomycetes in the stomach wall, liver, lymph-nodes, urinary bladder wall, omentum, appendix and ascitic fluid. This patient also had an ulcer of the stomach with the organisms in the ulcer wall. The conclusion was that the stomach wall was the portal of entry. From this it may be seen that the disease was quite widespread in the abdominal cavity and contrasts sharply with our patient who seemingly had a well localized infection. Harter[10] and Okake[11] also reported patients with widespread abdominal involvement.

CASE REPORT

P. W., a white, male, aged seventy-four, (Hospital No. 40-4456) was seen on April 20, 1940, by M. J. S. at his home. His complaints at that time were anorexia, vomiting at irregular intervals, abdominal distention, pain across

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the lower portion of the abdomen and alternating constipation and diarrhea. These symptoms had been present for ten days.

Physical examination revealed a tall, thin, patient, not acutely ill, with a moderate amount of abdominal distention and a tender movable mass in the right lower abdominal quadrant about the size of a lemon. Hospitalization was advised and on April 22, 1940, the patient was admitted to the hospital.

His past and personal history was not particularly significant. A complete recovery following a skull fracture in 1938 was noted, and a hemorrhoidectomy had been performed in 1930. He had lived in Chicago for the past forty years and was a building contractor.

On admission he appeared much the same as he did two days before at his home. The physical findings were essentially the same although a fever of 100°F. was observed. Urine analysis showed an occasional pus cell and epithelial cell. A blood count revealed the hemoglobin to be 10 Gm., erythrocytes 3,500,000 with slight anisocytosis, poikilocytosis, and polychromatophilia, leukocytes 9,600, of which 21 per cent were lymphocytes, 4 per cent large mononuclears, and 75 per cent neutrophils.

Roentgenographic studies were made on April 23, 1940, the day after admission to the hospital. The heart and lung fields showed no unusual changes. Barium enema revealed a redundant and tortuous colon. The right side of the colon was not well visualized and there appeared to be a filling defect corresponding to the site of the palpable mass (in the right lower quadrant), however, after evacuation and injection of air the appearance of the cecum and ascending colon was considerably changed. Therefore, it was decided to attempt to visualize the cecum by using barium per mouth on the following day. In addition to this change there were several large and small diverticuli in the sigmoid and ascending colon.

The next day, April 24, 1940, roentgenographic studies showed no intrinsic lesion in the stomach or duodenum. There was no delay in the passage of barium through the duodenum, and at four hours the stomach was empty with the barium distributed throughout the distal ileum and proximal portion of the colon. At this time there appeared to be a filling defect in the cecum corresponding to the site of the palpable movable mass. At twenty-four hours the same defect in the cecum was visualized and the inference by the roentgenologist was that a neoplasm of the cecum was present.

For the next few days attention was directed toward preoperative measures and on April 29, 1940, operation was performed.

Under inhalation anesthesia a right lower abdominal paramedian incision was made. A freely movable, hard, round, tumor mass about the size of an egg adjacent to the proximal portion of the appendix was palpable in the cecum. The appendix was short and thick and intimately adherent to the cecum. The anterior surface of the cecum was covered by omentum which was densely adherent. Suspecting that this segment of the adherent omentum indicated the presence of a threatened or actual perforation of the cecum, it was ligated and cut between two ligatures. Later examination of the specimen revealed a perforation 3 mm. in diameter underneath this adherent omentum. A resection of the cecum and ascending colon including the distal 10 cm. of the ileum was then effected. Blind-end closure of the transverse colon with an end-to-side ileocolostomy completed the intestinal surgery. One cigarette drain was placed in the colonic gutter and closure in layers performed.

The pathological report was as follows: The specimen consisted of 15 cm. of cecum, 10 cm. of ileum, and appendix. The bowel and appendix had been split open. At the base of the appendix there was considerable congestion and induration with ulceration and perforation on the anterior wall of the cecum. Microscopic sections reveal chronic granulomatous inflammation due to blastomycosis.

The postoperative course was quite uneventful except for a moderate amount of purulent drainage which persisted for approximately four weeks. At no time was fecal drainage noted. Fever which ranged between 99 and 100°F. was present for two weeks. The patient left the hospital thirty days after operation and soon regained his normal strength. He has had no symptoms referable to the gastrointestinal system following his recovery from the operation.

COMMENT

We believe that a separate, isolated infection due to blastomycosis in the cecum is of very rare occurrence. In fact, no other similar case has been reported to our knowledge.

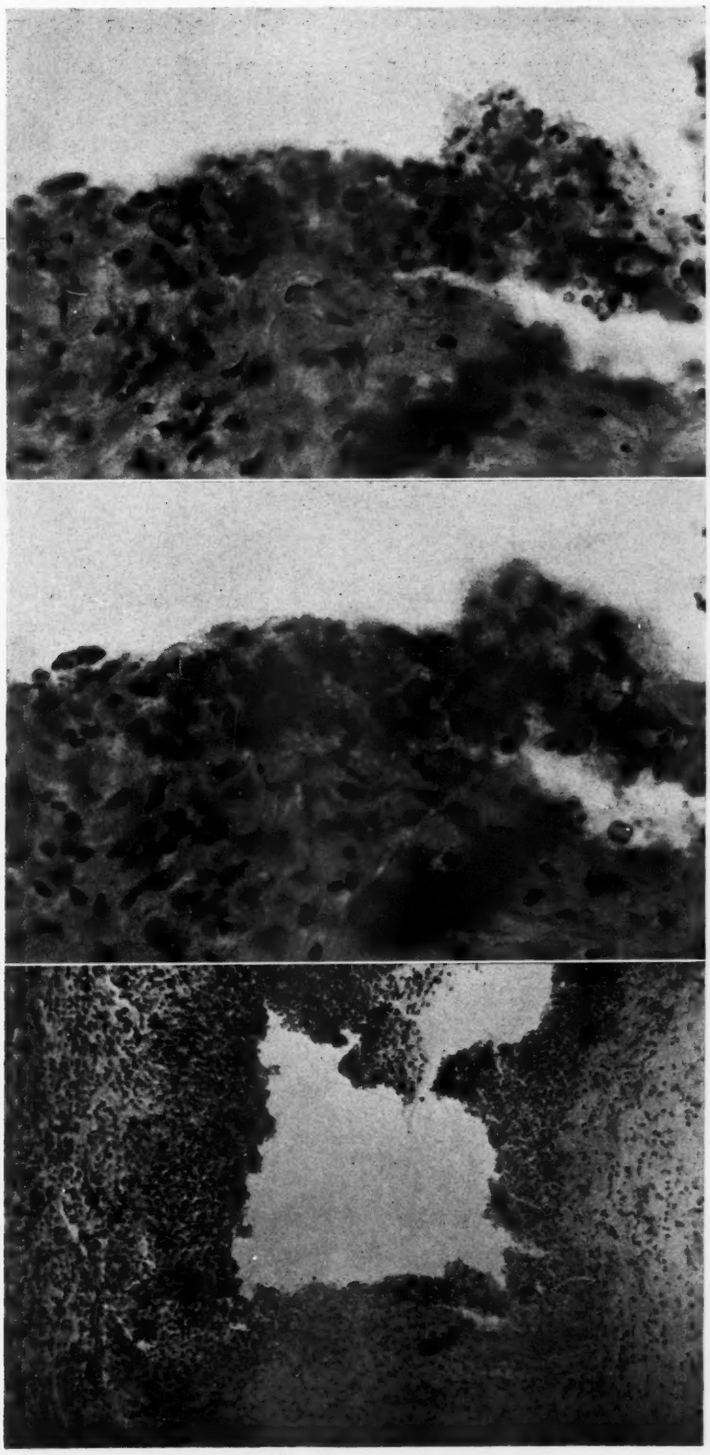

FIG. 1. A, photomicrograph of section of wall of cecum showing blastomycetes—× 630. B, photomicrograph showing spherical refractile (wall of cecum) blastomycetes—× 630. C, photomicrograph (low power) showing section of cecum; same as in A and B. × 155.

This patient has apparently been cured by a one-stage operation consisting of resection of the terminal ileum, cecum and ascending colon, and performance of an ileotransverse colostomy.

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Supernumerary breasts (polymastia) usually appear as small nipples below the breasts in the "milk line." Sometimes they are so small as to resemble pigmented moles. Occasionally miniature breasts are seen. Usually not more than one or two are present, but cases have been reported with as many as ten.

The brief excerpts in this issue have been taken from "Plastic Surgery of the Breast and Abdominal Wall" by Max Thorek (Charles C. Thomas).

SPLANCHNICOTOMY IN A SIX-YEAR OLD CHILD WITH MARKED HYPERTENSION*

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RELIEF of the distressing symptoms associated with far advanced hypertension has been shown to be a more frequent result of operations on the splanchnic nerves than is long standing lowering of the blood pressure.[1] It is believed, however, that even when there is little probability of increasing the life span of these unfortunate individuals, a procedure which permits them to spend their last days in relative comfort is justified. One of the criteria for the choice of subjects for surgery is the youth of the patient; with this case of a six-year old child we believe we are reporting the youngest individual on whom a splanchnic operation has been performed for hypertension.

CASE REPORT

A six-year old, white female entered the Children's Service of Cook County Hospital on March 10, 1940, with complaints of headache, vomiting and stiff neck of two days' duration. She was a lethargic, irritable child whose family gave a history of intermittent attacks of convulsions over a period of three years. Investigation showed that she had been seen sixteen times in the previous two years in out-patient clinics and had been hospitalized three times for convulsive attacks. Some of these started in the foot, spread to the arm and face on the same side and lasted from twenty minutes to two hours. Among the laboratory data uncovered from examination of her past history no blood pressure recording could be found. She had questionable positive Brudzinski and Kernig signs. The left pupil was slightly larger than the right although both reacted well to light. There was a loud, snapping aortic second sound and a systolic murmur heard best in the third left interspace. The liver was palpable two finger breadths below the costal margin. Blood pressure was 238/180 on all extremities. The urine consistently showed 4 plus albumin, with many cells and hyaline casts; specific gravity ranged from 1.010 to 1.020. The pressure of the spinal fluid was increased and there were 100 cells per c. mm. of fluid and a three plus pandy test. Hemoglobin was 14 mg., white blood count 18,400, blood nonprotein nitrogen 30 mg. and total protein 7.81 mg. (albumin-globulin ration was 6.25/1.56. *X*-rays of chest, abdomen and skull were negative and on March 27 a retrograde pyelogram was normal. Eye-ground examination showed several small areas of degeneration. The vessels were small but no "crossing phenomena." Cystoscopy reported hypertrophy of interurethral ridges with bulbous edema of both ureteral orifices. The patient did not derive benefit from treatment with magnesium sulfate or hypertonic fluids but remained semicomotose, incontinent and vomited frequently, so a splanchnicotomy was suggested and performed by Dr. Verbrugghen.

The left side was done on April 5 and the right on April 19. The patient developed a right upper lobar pneumonia following the second operation but recovered uneventfully and her blood pressure which had never been below 200/160 preoperatively, gradually fell to 160/110 by May 5, and then began to rise again. Symptomatically she was much improved, more alert, cheerful and bright, with only occasional nausea and no vomiting. By May 16, although her blood pressure was 190/120, her general condition was excellent and plans were made to send her home. At this time her urine showed 1 to 2 plus albumin, with specific gravity varying between 1.007 and 1.013 and her blood nonprotein was 35. She began again to vomit and ran a steady downhill course, became stuporous and expired June 8, 1940.

Postmortem examination revealed a poorly developed, poorly nourished, white female, 127 cm. in length and weighing 20 kg. There were two recent surgical scars over the back at the

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level of the eleventh thoracic vertebra bilaterally and a supernumerary digit on the left foot. The pericardial sac contained about 40 cc. of clear yellow fluid. The heart weighed 180 Gm. The myocardium was very firm and the wall of the left ventricle measured 16 mm. and the right 4 mm. in thickness. There were many small fatty and hyaline placques on the membranous endocardium of the left ventricle, the free margins of the aortic and mitral valves were slightly thickened and the left ventricle was moderately dilated. The coronaries and aorta were essentially negative. There was a chronic passive congestion of the liver, spleen and an aberrant spleen. The latter measured 26 by 15 by 12 mm. The kidneys weighed 165 Gm. together. The left was slightly smaller than the right. The capsule stripped with slight difficulty leaving a coarsely granular, light purple and grayish tan surface with an occasional depression 6 mm. in length and 2 mm. in depth. On sectioning, the cortex averaged 4 mm. in width, was light purplish tan and the markings were distinct. The medulla appeared to be normal. Both renal arteries measured 3 mm. in diameter at their points of origin.

The vagina was divided into two separate and distinct parts by a thick, firm, longitudinal septum. Each vagina connected with a separate and independent cervix and uterus. Each uterus had only one tube. (Double vagina and bicornuate uterus.) The uterus measured 33 by 15 by 7 mm. Both Fallopian tubes were patent and the ovaries were small. The thyroid, pancreas, adrenals and pituitary were essentially unchanged. The brain weighed 1,060 Gm., it was edematous, the convolutions were flattened, the meningeal vessels were congested, and there were small multiple intermeningeal hemorrhages over the frontal and occipital lobes. The left lateral ventricle was moderately dilated and contained about 30 cc. of clear fluid. The third ventricle appeared to be normal. The white matter was congested. The vessels at the base of the brain contained scattered fatty and hyaline placques.

Microscopic examination revealed a slight perivascular, round cell infiltration in the meninges and white matter and a moderate hyperplasia of the intima and media of the arteries and arterioles in both the meninges and cortex. The general cyto-architecture of the cortex was preserved and no significant gliosis was noted.

Muscle fibers of the heart were markedly hypertrophied, cross striations were indistinct, cytoplasm was light pink and granular and the nuclei were barrel shaped.

The architecture of the kidney was well preserved. The glomeruli were swollen and filled Bowman's capsule. There was slight to moderate proliferation of the endothelial cells of the capillary tufts and the latter were moderately congested with red blood cells. There were several partially to completely hyalinized glomeruli scattered throughout and an occasional epithelial crescent was present. Bowman's capsule was slightly to moderately thickened. The interstitial capillaries were markedly dilated and filled with red blood cells. The tubular epithelium was swollen and granular and the lumina contained cellular débris and numerous hyaline casts. The small arteries and arterioles showed marked thickening of the intima and media, some to the point of occlusion of the vessel, and there was a moderate increase in interstitial connective tissue. There were focal accumulations of round and plasma cells, especially near the hyalinized glomeruli. Sudan III stain revealed a moderate to marked deposition of sudanophilic droplets in the tubular epithelium, the hyalinized glomeruli and in the intima and media of the small arteries and arterioles.

Microscopically the pituitary, thyroid and adrenal gland were normal.

The anatomical diagnosis was as follows: Chronic glomerulonephritis; marked eccentric hypertrophy of the heart with dilatation of all cardiac chambers; slight fibroplastic deformity of the aortic and mitral valves; marked edema and passive congestion of the brain and moderate internal hydrocephalus on the left side; passive congestion of the lungs, liver, spleen and kidneys; parenchymatous degeneration of the heart, liver, and kidneys; stasis catarrh of the gastrointestinal tract; uremic injection of the small intestine; bicornuate uterus and double vagina; aberrant spleen; supernumerary digit of left foot; recent healed surgical scars at level of eleventh thoracic vertebrae bilaterally.

DISCUSSION

Splanchnicotomy was first introduced for the relief of hypertension by Pende,[2] in 1924, and according to Martin's compre-

hensive review of the literature[3] "is rapidly growing in popularity and if one may judge by results stated in reports, is offering more hope for a solution than any form of surgery yet described." Craig and Allen[4] as well as many other authors have pointed out that in far advanced cases the effect of surgical procedures is neither marked nor lasting. However, the extent to which symptoms are relieved, as reported by Crile[5] and others, would seem to justify the procedure in selected cases, especially since the mortality is very low. Although the kidney is apparently the chief etiological factor in a large proportion of cases, Mosenthal and Lander[6] have shown that it is difficult to determine whether the hypertension is primary or secondary to the renal picture. Keith et al.[7] believe that vasoconstriction is the constant factor in the different types of hypertension. Even though developmental anomalies were presented in this case, we do not believe that they contributed to the cause of the hypertension. However, it is possible that some further anomalous condition may have escaped detection at autopsy especially since no examination of the spinal cord could be made, and the renal pathological status might have been secondary to hypertension caused by such a condition.

SUMMARY AND CONCLUSION

A case of a six-year old girl with a three-year history of convulsions and a blood pressure of 238/180 was temporarily symptomatically improved by bilateral splanchnicotomy. This is the youngest recorded case of its kind.

Splanchnicotomy may give symptomatic relief in far advanced cases of hypertension due to chronic nephritis.

Blood pressure readings should be taken in all children subject to convulsive attacks.

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DOUBLE MALIGNANCY: HYPERNEPHROMA AND BASAL CELLED CARCINOMA OF NOSE*

REPORT OF CASE

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THE multiplicity of primary malignant tumors occurring in different organs of the body is of great interest to the medical world. We report a case of multiple cancer in which nephrectomy was performed for hypernephroma. Three years later the patient developed basal celled carcinoma of the nose requiring removal. The cancerous lesions involving the kidney as well as those of the nose presented the characteristic pathological picture of well recognized neoplasms that commonly involve these organs. There was no metastasis from either primary cancer and each was individually cured by radical extirpation of the kidney and of the nose. By virtue of a series of plastic operations the nose has been entirely reconstructed. Over a period of fourteen years there has been no recurrence of kidney cancer nor any evidence of metastasis to other organs. The patient has not only been definitely cured of cancer and restored to good health but her nose has been so well reconstructed that she is now a presentable member of society. This case is indeed a living testimonial to the efficacy of radical surgical removal of cancer when it is found to exist in the vital organs of the body.

A number of cases presenting multiple cancer have been published. In 1940, Shapiro and Bolker reported an interesting case presenting co-existent triple primary neoplasms consisting of lymphosarcoma of the right inguinal region, adenocarcinoma of the right kidney and papillary adenocarcinoma of the colon. White explains the genesis of primary multiple cancers on the basis of the interaction of a functionally matured gene bearing the unit character for cancer inheritance with a functionally matured gene bearing the unit character for localization in various structures. He points out the fact that in cases of multiple cancer there must be definite, distinct and invasive new growths presenting the macroscopic and microscopic characteristics of the morphologic features of independent cancers, the cells of each type being equally capable of forming characteristic metastasis.

CASE REPORT

A female, aged thirty-six, Case No. 49547, referred by Dr. Wm. Fritschen, entered St. Mary's Hospital January 4, 1928, for diagnosis and treatment of painful swelling in the left upper abdominal quadrant. In 1914, she suffered from general debility. This continued and in 1924 appendectomy was performed without improvement of her condition. In 1924, the patient underwent cholecystectomy for cholecystitis. In 1927, she noted fullness in the left upper abdominal quadrant and lumbar region. Since that time she suffered from dull nonradiating pain in the left loin. At times there would be nausea but this was not accompanied by vomiting. She noted hematuria on two occasions and, other than occasional nycturia, she complained of no other urological symptoms. The patient ran an intermittent fever, the temperature varying from 98° to 101°F.

The heart and lungs were negative. In the upper left abdominal quadrant a smooth tender mass was palpated. It extended into the kidney fossa and moved freely with respiration.

* From the Departments of Urology and Plastic Surgery, Saint Mary's Hospital, San Francisco, California. Read before the monthly clinical staff meeting of St. Mary's Hospital, San Francisco, September 18, 1941.

Laboratory examination of the blood revealed the following: hemoglobin, 85 per cent; erythrocytes, 4,790,000; leukocytes, 14,500; small lymphocytes, 14; monocytes, 10; and neutrophiles, 76. The blood Wassermann test was negative.

FIG. 1. Ureteropyelogram showing marked distortion of the kidney pelvis. In addition to elongation and to pressure defect of the lateral border of the upper major calyx there is extravasation of the opaque medium into an irregular cavity involving the upper pole.

FIG. 2. Photograph of sagittal section of kidney removed by operation demonstrating large hypernephroma of the left kidney containing a large necrotic cavity.

The urine was found to be turbid; reaction, acid; specific gravity, 1.027; albumin, trace; and sugar, negative. Microscopic examination revealed heavy strands of mucus, 4 to 6 leukocytes to the high dry field, erythrocytes 50 to 60 to the high dry field and no organisms. Phenolsulphonephthalein test (intramuscular) 80 per cent of the dye recovered in two hours.

A complete kidney examination was made including cystoscopy, catheterization of the kidneys, renal function tests and microscopical examination of the urines including cultures. Our studies revealed moderate staphylococcic infection of the left kidney and bladder as well as diminished function of the left kidney.

In addition, a roentgenological examination was made. Fluoroscopy of the heart and lungs and *x*-ray films of the gastrointestinal tract revealed negative findings. Flat kidney films showed considerable irregular enlargement of the left kidney. Bilateral retrograde pyelograms were made. The right kidney pelvis appeared normal. The left kidney pelvis presented considerable distortion. (Fig. 1.) The upper major calyx was irregular and elongated and presented a pressure defect of the lateral wall. It communicated with an irregular cavity involving the upper pole measuring 4 cm. in diameter. The middle calyx was considerably elongated and flattened and extended laterally for a considerable distance. In taking the pyelogram in the upright position, considerable descent of both kidneys was observed.

The diagnosis of cancer of the left kidney was made and it was decided to carry out nephrectomy immediately. In reviewing the pyelograms we endeavored to explain the cavity that existed in the upper pole of the left kidney. This could well have been due to abscess formation, in view of the leukocytosis of 14,500 and the fact that the patient was running a fever. In studying the pyelogram taken in the vertical position it was noted that there was an appreciable descent of the kidney. The absence of renal fixation—the author's (Mathé) positive roentgenographic sign for kidney and perinephritic abscess—ruled out suppuration in the renal parenchyma in this case.

Nephrectomy was performed on January 20, 1928, through the usual lumbar incision. The kidney was found to be considerably enlarged, about three times its normal size, due to a tumor involving the upper pole. The renal pedicle was deliberately clamped early in the

operation and the kidney carefully dissected free from the surrounding tissues in order not to force any of the cancerous cells into the renal vein nor to spill them into the incision. During the operation the tissues were gently handled and the wound was repeatedly washed with alcohol. The renal pedicle was triply tied *en masse* and the kidney removed.

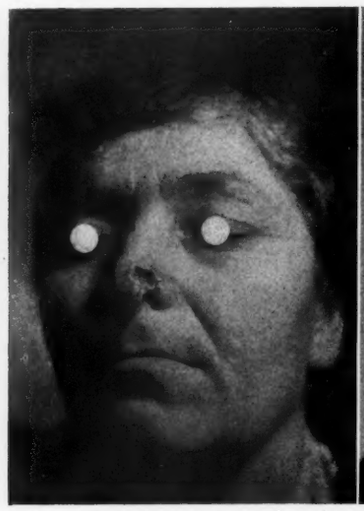

Fig. 3. Basal cell carcinoma of the nose; duration approximately eight years. Surgery advised at this time, December, 1939, but treatment refused.

Fig. 4. Showing the appearance of the carcinoma in August, 1940. Radium therapy has failed to control extension of the tumor.

Dr. Elmer Smith, pathologist, St. Mary's Hospital, reported the following findings: "The kidney presents a large yellow tumor of the upper pole, the center of which contains a necrotic cavity. The tumor mass exerts considerable pressure on the upper pole, almost completely replacing normal kidney tissue. The lower portion of the kidney appears normal. Microscopical sections of the tumor reveal that it is composed of fibrous-like tissue made up of spindle cells which have invaded the cortical substance of the kidney, causing almost complete atrophy of the tubules. A few tubules still remain in this region, however, they are markedly compressed. There are a few epithelial structures which appear to be active and resemble young glandular tissue. Reticulated round cells are found in that part of the margin of the tumor mass that has not undergone necrosis and contains a few leukocytes and wandering cells as well as blood pigment. In the margin, between the actively growing tumor and the necrotic area, one sees many dilated capillaries and hemorrhagic areas such as are often encountered in the line of demarcation between necrotic and actively growing tissue. The structure of the tumor near the kidney capsule resembles fibrosarcoma; however, small reticulated cells with small nuclei resembling those of the adrenal body are also present. Diagnosis: hypernephroma of the left kidney."

The wound healed in thirty days after which time the patient was given a course of postoperative radium therapy consisting of 5,000 mg. hours and discharged from the hospital free of pain and fever. While preparing a paper on cancer of the kidney, which was delivered before the Urological Section of the California Medical Association Meeting in May 1936, the patient was contacted in Chicago, Illinois, at which time recheck investigation revealed that she had been entirely relieved of her symptoms and was enjoying perfectly good health.

In 1932, the patient noted a small pimple on the nose which gradually increased in size and became ulcerated. Ointments were applied with no relief. In 1938, she consulted Dr. Monica Donovon who made a diagnosis of basal celled carcinoma and instituted radium therapy. After primary regression, radium seemed to lose its effectiveness and the carcinoma soon invaded the greater portion of the nose. Dr. Donovon, who has had wide experience in radium therapy, then advised surgical extirpation.

In December, 1939, one of us (C. F. S.) was called in consultation for the purpose of

surgically relieving this condition. At this time the tumor had involved the greater portion of the nose. (Fig. 3.) Biopsy revealed a typical basal celled carcinoma. Careful examination showed that there was no metastasis in the neighboring glandular structures, however, the nasal lesion had extended into the alar cartilage, septum and columella. Surgical extirpation and subsequent plastic repair of the nose was recommended; however, the patient refused radical surgery and requested another course of radium therapy. This was instituted with the understanding that if there was no improvement, surgical intervention would be carried out.

Fig. 5. Appearance of nose following surgical excision of the tumor. The forehead flap has been raised and delayed. Note the unfortunate pre-existing forehead scars.

Fig. 6. Appearance of the nose at the present time. Further work will be done to improve the cosmetic result. The forehead defect has been grafted with full thickness skin.

In September, 1940, the patient was re-examined and it was observed that considerable growth of the cancer had taken place. (Fig. 4.) Fortunately, the palpable glands of metastasis were still absent and it was agreed to relieve this condition by surgical intervention with a full understanding of the radical nature of this procedure. A simple plan of attack was decided upon, namely, wide excision of the malignant lesion with disregard of consequent defect. After healing had occurred reconstruction surgery would be carried out, utilizing all available material and according to existing circumstances.

On September 16, 1940, under avertin and local anesthesia, the tumor was excised widely with the electric knife, including two-thirds of the nose and a portion of the septum and the columella. The mucous membrane of the nose and the skin were sutured together at the margin of the defect that had been created thus forming a closed wound. The patient made an uneventful recovery, the wound healed in four weeks, at which time the surgical problem of reconstruction was undertaken. (Fig. 5.)

We were now dealing with the problem of complete rhinoplasty since both the skin of the nose as well as its nasal lining had to be provided. As the patient was very nervous, a rapid and comfortable type of reconstruction operation was chosen, namely, the forehead flap. We elected this method of repair in spite of the fact that there were pre-existing scars on that portion of the forehead that was to be utilized in the flap and which would necessarily have to be transplanted to the nose. The first stage of this reconstructive operation consisted in the formation of a forehead and scalp flap that was formed in such a way that its pedicle would contain the right temporal artery. This flap was not immediately brought down to the nose, but was deliberately delayed by returning it to its original bed for the purpose of allowing the circulation to adjust itself. At the time of operation, flaps were also resected from the margin of the defect produced by removing the nose and these were turned inward in order to furnish a lining. These flaps were also delayed.

Three weeks later, the second stage of the operation was performed. This consisted of again raising the lining flaps and suturing them

to the freshened edges of the defect. The forehead flap was then superimposed on these lining flaps and sutured into place, forming the nostrils and columella with infoldings of pliable skin. The defect in the forehead formed by removing the flap was corrected by grafting a suitable sized portion of full thickness skin of the abdomen. (Fig. 6.)

Three and a half weeks later, the pedicle was severed and the scalp flap replaced into its original bed. In the meantime the full thickness graft had taken completely. After healing had occurred, a better cosmetic result was obtained by performing minor surgical adjustments which were deemed necessary. The pre-existing forehead scars can still be seen but the final result is indeed successful, inasmuch as the cancer has been completely removed and the nose has been successfully reconstructed.

DISCUSSION

This patient presented an unusual condition in the fact that she was afflicted by different types of cancer, viz., hypernephroma of the left kidney and basal celled carcinoma of the nose occurring independently and three years apart. She was cured of cancer by nephrectomy for hypernephroma in 1928 and by radical removal of the nose for basal celled carcinoma in 1940. She has shown no evidence of recurrence of kidney cancer in fourteen years. We realize that metastasis from renal neoplasms occasionally take place as long as twelve years after surgical removal, however, one can justly conclude that this patient has been definitely cured of kidney cancer because she is living and well fourteen years after nephrectomy. The basal celled carcinoma of the nose failed to respond to radium therapy and was successfully relieved by radical excision, and the nose was subsequently reconstructed by a series of plastic operations. The patient has been restored to good health and is now a presentable member of society.

SUMMARY

1. We report a case presenting double primary neoplasms consisting of hypernephroma of the left kidney and basal celled carcinoma of the nose occurring independently and three years apart.

2. The patient presents a fourteen-year cure of kidney cancer. Early ligation of the renal pedicle, gentle handling of the kidney and sponging of the wound with alcohol sponges during nephrectomy and utilization of postoperative radium therapy aided in curing this patient.

3. The basal celled carcinoma of the nose, which had responded to radium therapy for a time, became radioresistant and required radical extirpation.

4. The nose has been successfully reconstructed by a series of plastic operations.

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AVULSION OF THE ANTERIOSUPERIOR ILIAC SPINE*

ASSOCIATED WITH OSTEOCHONDRITIS AND HYPOTHYROIDISM

ROSS SUTHERLAND, M.D.
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AND

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FRACTURES due to muscular force alone and particularly those of avulsion of the anteriosuperior iliac spine are relatively rare. The possibility of predisposing bone weakness as an etiological associate of muscular violence has not, to our knowledge, been proposed.

CASE REPORT

Our patient, a boy of fifteen, had been treated in this clinic several years previously for mild osteochondritis of the calcanei and spine with thyroid medication. He had failed to return after subsidence of symptoms until two years ago. At that time he gave a history of sprain

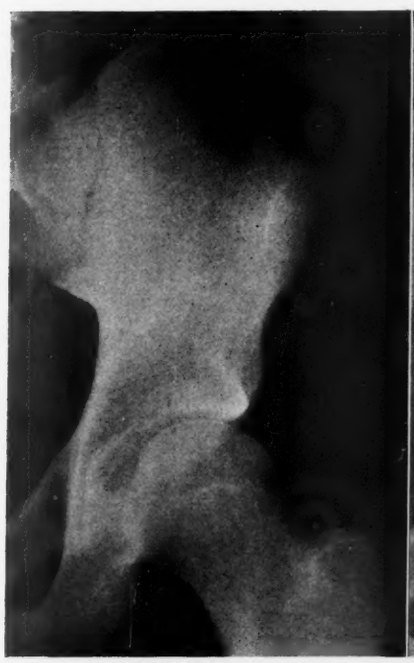

FIG. 1. Original film showing fracture.

FIG. 2. Film three weeks postoperatively.

FIG. 3. Spine film showing irregularities due to osteochondritis.

* From the Tichenor Orthopedic Clinic, Long Beach, California.

of the left ankle several weeks previously, which pain had not entirely subsided. *X*-rays revealed fracture of the left talus but clinical limitation of motion and pain were relatively slight, so surgical treatment was delayed until the condition warranted further therapy. He then did not return to the clinic or continue his thyroid medication until the present injury. At this time he was running, fell to the ground with a sudden severe pain in the left hip area and was unable to arise. There was marked tenderness over the fractured left iliac spine, crepitus was elicited and *x*-rays confirmed the diagnosis.

He was put to bed and seven days later because of continuing disability an open reduction was done of the separated fragment which was fixed in place with a vitallium nail and a mattress suture. A spica bandage was applied and he was kept in bed for three weeks. At that time the wound was well healed, full muscle function was present and painless, and callus was visible in the *x*-ray.

Laboratory studies made four weeks postoperatively were as follows:

Basal metabolic rate: −5 per cent on two separate determinations
Blood cholesterol: 168.2 mg. per cent. (Two years before while under thyroid therapy the blood cholesterol was 127 mg. per cent)
Blood calcium: 5.59 mg. per cent
Blood phosphorus: 3.91 mg. per cent
Blood phosphatase: 8.59 units
Blood sedimentation rate: 8 mm. in sixty minutes

Thus in this case there is mechanical inbalance in the leg from a distorted talus causing muscular violence which produces a fracture in an epiphysis having probably delayed growth and abnormal endocrine status which is substantiated by the lower basal metabolic rate. This endocrine factor may be the underlying cause in some of the fractures which are now given as caused solely by muscular violence.

REFERENCE

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GALLBLADDER FORCEPS FOUND IN THE ABDOMINAL CAVITY

CASE REPORT

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ROCHESTER, NEW YORK

NUMEROUS cases have been reported of foreign objects found in the abdominal cavity days or months after an operation. In this patient, gallbladder forceps were found two years after the removal of the gallbladder. The patient was fairly comfortable until three weeks before entering the hospital. Her chief complaint was a sharp, griping pain on the right side near the costal margin radiating across the abdomen, one to two hours after meals. Fat did not increase the pain. The patient stopped eating fat on the advice of a physician. She was afraid to eat for fear pain would increase. Soda bicarbonate did not give any relief. The last four days, the pain was constant and accompanied by nausea and vomiting.

Physical examination showed an obese woman, fifty-seven years of age, acutely ill and in distress. The abdomen was very obese and difficult to examine. Tenderness was present more on the left side than on the right. No spasm or rigidity was evident, but there was question of an ill defined mass in the right upper quadrant. No fluid or distention was present. A questionable liver edge could be felt three fingers below the costal margin. A small ventral hernia was present. A flat *x*-ray of the abdomen showed a large gallbladder clamp within the abdominal cavity.

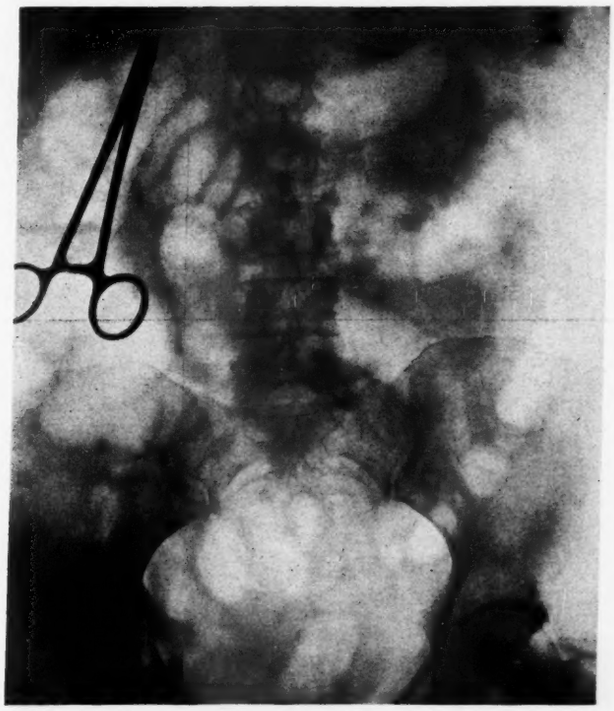

FIG. 1. Forceps in abdominal cavity.

Operation revealed a large gallbladder clamp, still locked, completely buried and surrounded tightly by adhesions which had to be cut. It was impossible to open the clamp *in situ* before removing it. The hernia was repaired and the patient made an uneventful recovery. To this date, she does not know that she had the gallbladder clamp in her abdomen for two years.

Selected Book Reviews

THE first edition* of "Disability Evaluation—Principles of Treatment of Compensable Injuries" came out in 1936. As the author states, "(It) was a venture into a somewhat untrodden textbook field." The author undertook (and successfully) to clarify the subject of physical disability as it pertains to economic loss to labor and industry.

There was a healthy response to this new work and a second edition was published two years later. The book continued to enjoy wide popularity and now the third edition, which has been thoroughly revised with added material through suggestions arising from physicians, lawyers and industrial courts, is offered the profession.

To quote Dr. McBride: "The composite schedule of disability evaluations included in this edition was formulated after a great deal of investigation. Such existing rating schedules as that of the United States Veterans' Administration and other legalized standards were used as a pattern. The percentages and principles of rating disabilities, as cited in this table, are therefore based on medical opinion, supported by legal and statutory experiences. A reasonably definite standard of average ratings is thus presented to provide a ready reference in formulating decisions and opinions as to the evaluation of disability."

There is a new chapter on the responsibility of the doctor as an expert witness. After a chapter on basic surgery, chapters follow on the subjects of workman's compensation laws, standardizing medical evaluation of disability, the procedure of analysis in evaluation of disability, examination of the disabled person, joint stiffness, chapters on ankylosis of the shoulder joint, elbow joint, wrist joint, the hand as a unit, the fingers, the hip joint, the knee joint, ankle joint, and the toe joints, chapters on the disability of fractures, fractures of the clavicle, scapula, humerus, forearm, carpus, metacarpus and phalanges, pelvis, femur, tibia and fibula, the tarsal bones, the industrial back, the trunk, nerve injuries, amputations, head injuries, injuries of the eye, injuries of the ear, burns and hernia.

* Disability Evaluation—Principles of Treatment of Compensable Injuries. By Earl D. McBride, B.S., M.D., F.A.C.S. Third Edition Revised. Philadelphia, 1942. J. B. Lippincott Company. Price $9.00.

The book numbers 631 pages and there are 374 illustrations. There is also a bibliography and an ample index.

To all physicians engaged in this type of work this valuable book is seriously recommended.

"The Principles of Anatomy as Seen in the Hand"* appeared originally during the first World War in 1914. It was written, as the author tells us, because the many war injuries that involved the functional use of the hands in civilian life formed at that time an outstanding problem in the passage of discharge from military service. Therefore, "It seemed obvious that no proper assessment of military disablement could be translated into terms of civilian disability unless the functional anatomy of the hand was properly realized. This resulted in a series of lectures as a part of the course of instruction of officers of the R.A.M.S.C. at the Special Military Surgical Hospital, Shepard's Bush." Naturally, this edition was out of print and out of date for many years. Therefore, a new edition was practically rewritten which includes six new chapters and twenty new illustrations.

Written by the Professor of Anatomy, at the University of Manchester, the book is fundamentally and scientifically sound. Added to this a freely flowing style makes a rather dry subject interesting and engaging.

The illustrations are good. There is an unstinted bibliography for those who wish to delve deeper into the subject and the index of subjects is also ample.

In these times every surgeon in civilian practice and, above all, every surgeon in the armed forces, would do well to give this work on the "Anatomy as Seen in the Hand" his serious attention.

The treatment of burns offers debatable aspects. Many years ago the problem was settled by the housewife who rubbed lard on her scalded child. Decades passed and in the laboratory research workers attempted to determine the exact nature of burn "toxemia." There is a wide gulf and lack of adjustment between the two. Dr. Harkins has presented all sides of the question, and in the writing of his monograph† has contributed a great deal. Anyone who reads "The

* The Principles of Anatomy as Seen in the Hand. By Frederick Wood Jones, D.SC., F.R.S., F.R.C.S. Second Edition. Baltimore, 1942. The Williams & Wilkins Company. Price $7.50.

† The Treatment of Burns. By Henry N. Harkins, M.S., M.D., PH.D., F.A.C.S. Springfield, 1942. Charles C. Thomas. Price $6.50.

Treatment of Burns" is sure to view the subject from a new and broader viewpoint.

This comprehensive work on burn therapy concerns itself with pathology, chemistry and blood concentration. It deals with primary and secondary shock, the rôle of the adrenals, of fluid loss, of toxins and of bacteria in burns. We learn of the early and late complications in burns, of general and local treatment, of the new discoveries and of recent international developments. Burns disfigure; hence early and late plastic treatments are considered. Special burns, regional burns, electrical and radiation burns, chemical burns, and freezing, as well as war burns and industrial burns are all included in this text.

Today a book of this character is timely and needed. It is well written; the publisher has given us a good book to look at and to hold. It is nicely illustrated, contains a lengthy bibliography and an index of both authors and subjects.

Richard C. Cabot, late Professor of Clinical Medicine, at Harvard University, first published his "Physical Diagnosis"* in 1900. Since then twelve editions and many reprintings have come off the press (the twelfth edition was by Cabot and Adams), and now the thirteenth edition is by Dr. Adams. What Doctor of Medicine, graduated during the last forty years, does not know of Cabot's Physical Diagnosis? (It is hard for us to say Cabot and Adams "Physical Diagnosis" by F. Dennette Adams, but, no doubt, in time we will learn.) The writer bought a copy while a medical student about thirty-six years ago. It fascinated him. He has owned and used other editions since then.

Something "new has been added" to each new edition. Medicine does not stand still, and the first "Physical Diagnosis" seems an anemic little thing alongside this new 888-page volume. We do not review this "standard" in order that you make its acquaintance; we are simply telling you that Dr. Adams has revised and brought up to date this old friend. Much new material has been added; many sections and passages have been rewritten and the illustrative material has been modernized by replacing many of the older illustrations with better ones. The publishers write on the jacket that "it will continue to be the first choice of teachers." Perhaps, after all, this is only a mere statement of fact. We are happy this old friend is still with us.

* Cabot and Adams Physical Diagnosis. By F. Dennette Adams, M.D. New Thirteenth Edition. Baltimore, 1942. The Williams & Wilkins Company. Price $5.00.

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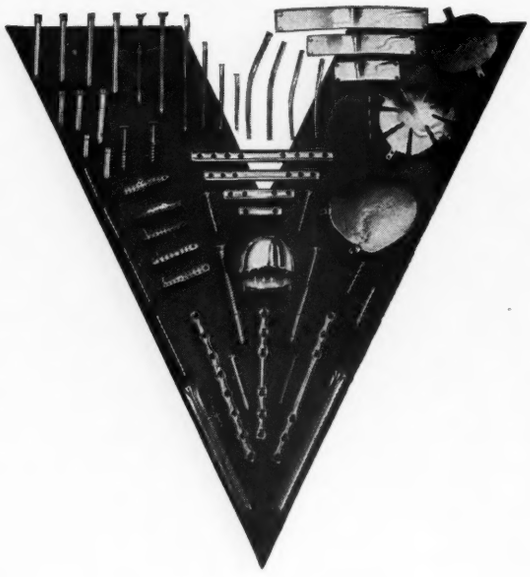

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*Campbell, W. C. and Speed, J. S., Annals of Surgery, 110-1. July, 1939. • Berry, H. C., Journal of Arkansas State Dental Association, 10-2. June, 1939. • Strock, A. E., American Journal of Orthodontics & Oral Surgery, 25-5. May, 1939. • Doherty, W. B., American Journal of Ophthalmology, 22-4. April, 1939. • Smith-Petersen, M. N., The Journal of Bone & Joint Surgery, 21-2, April, 1939. • Claflin, R. S., American Journal of Orthodontics & Oral Surgery, 25-1. January, 1939. • Hopkins, H. H. and Zuck, F. N., Medical Bulletin of Veterans' Administration, 15-3. January, 1939. • Venable, C. S. and Stuck, W. G., Journal of American Medical Association, 11-15. October 8, 1938.

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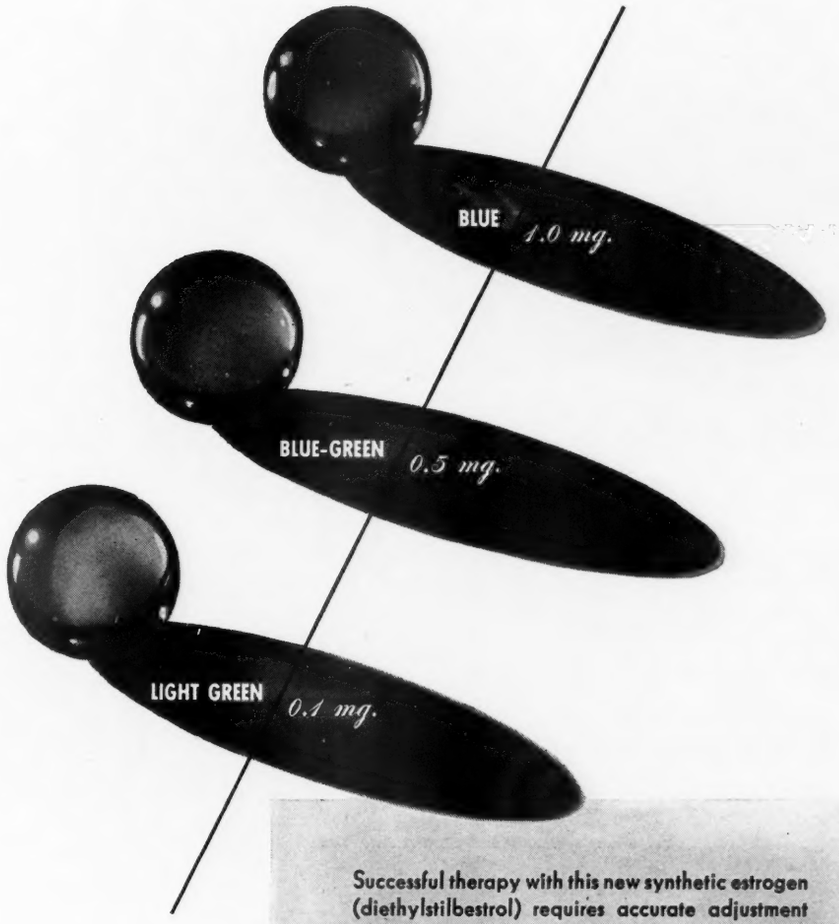

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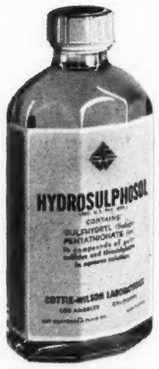

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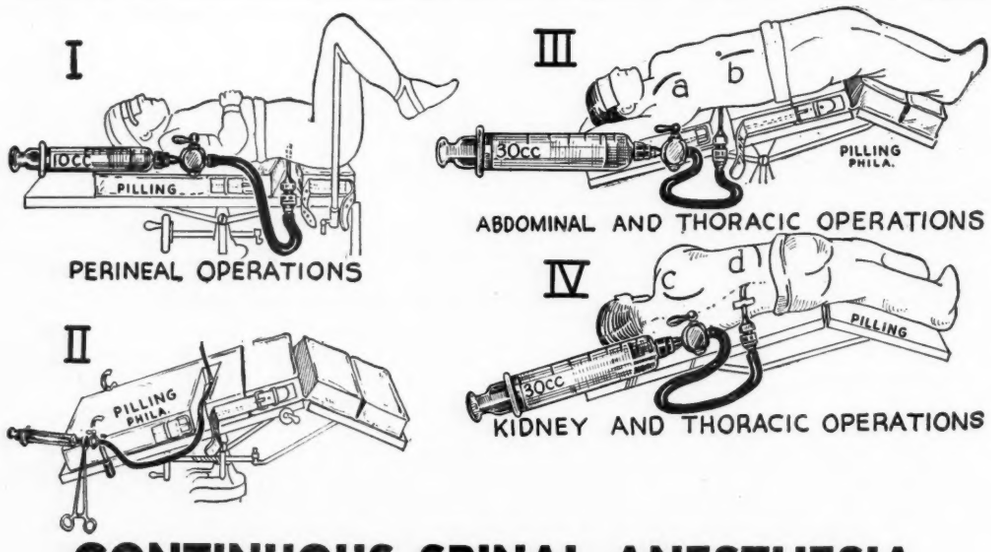

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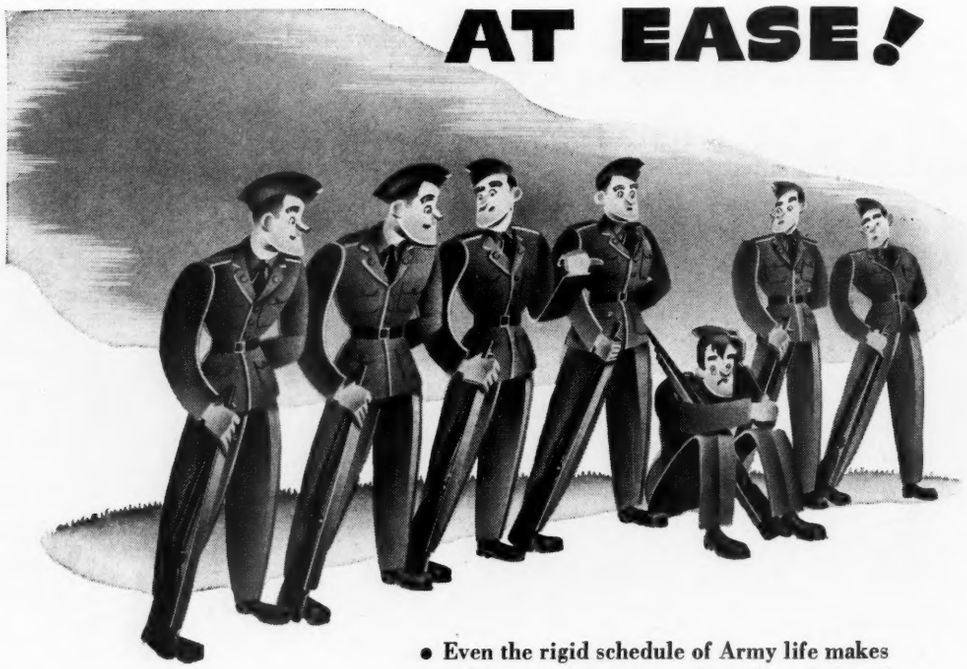

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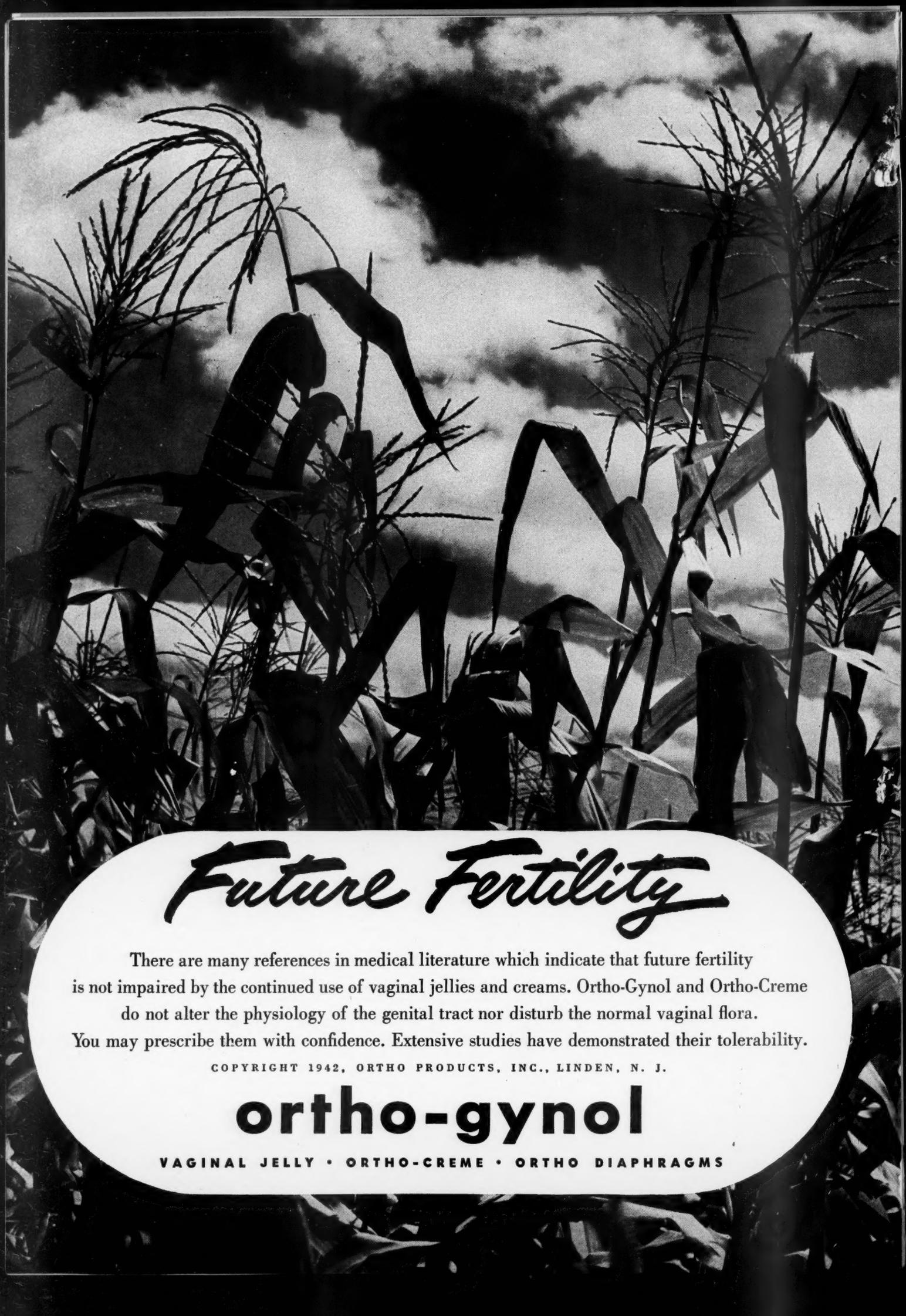

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